

Evidence-based Management of the Cat with 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, it is characterised by dysuria (painful or difficult urination), pollakiuria (frequent and/or prolonged attempts to urinate), stranguria (straining to urinate), haematuria, excessive licking of the genital area and/or periuria (voiding outside the litter box). FLUTD leads to inappropriate urination which affects the family-cat bond and is a common reason why cats are relinquished to shelters¹.

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^{2,3,4,5}. The diagnosis of feline idiopathic cystitis is dependent on exclusion of other known causes of lower urinary tract signs⁶. Urinary stones or uroliths, are another common disorder accounting for 15-23% of cases^{2,3,4,5}. Uroliths can form if the urine is supersaturated causing formation and growth of urinary crystals. Blockage of the urethra may be caused by either uroliths or matrix-crystalline plugs which are diagnosed in approximately 10-21% of cats with FLUTD^{2,3,4,5}. However, since urethral plug formation occurs almost exclusively in male cats, the true prevalence in the population at risk is much higher (> 40%).⁷ In 2010, 90% of urethral plugs analysed at the Minnesota Urolith Centre were composed of struvite while < 1% were calcium oxalate⁸.

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, 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. Environmental risk factors that have been identified include living in a multi-cat household, living indoors (or having restricted access to outdoors) and/or having

to use a litter tray^{9,10}. 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 sample should also be non-refrigerated urine and stored in an enclosed container. Cooling or refrigeration may enhance crystal growth, 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 large time 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 there is variability using the test strips.
- Specific gravity measures the urine concentration and assesses whether water is being secreted or conserved appropriately. 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 USG's are encountered in healthy animals, however, values encountered typically for normally hydrated cats are 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 maybe 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 indicator 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 radiography is a valuable diagnostic tool 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 by survey radiography as are radiopaque uroliths < 2-3 mm in diameter. Abdominal ultrasound is a useful tool to diagnose uroliths in the bladder, assess bladder wall thickness and differentiate blood clots from uroliths.

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 and 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 the long-term management of the most common conditions 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, reducing free radical damage and 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 pH when it is 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 to 6.4¹¹. A study of 10 healthy adult cats and 11 stone-forming adult cats demonstrated the relationship between urine saturation (for struvite and calcium oxalate) and urine pH¹². 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. Urine pH was found not to be as significant a factor for calcium oxalate urine saturation. However, a study showed that cats fed foods designed to produce urine pH of 5.8 to 6.29 was associated with increased risk of calcium oxalate uroliths¹³. In another study, cats fed foods designed to produce urine pH of 5.99 to 6.15 were 3 times more likely to have calcium oxalate uroliths than cats fed foods to maintain urine pH of 6.5 to 6.9¹⁴.

Increasing water intake leads to an increase in urine volume and production of more dilute urine. The concentration of minerals in dilute urine is decreased which is beneficial for urolithiasis. Also, because there is an increase in urine volume, there will be a need to urinate more frequently thus urine will be less likely to be retained in the bladder which is 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. 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 to increase water intake in cats, some cats will not eat canned foods, or some owners prefer not to feed canned foods. Thus, increasing water intake must be approached by other means.

One proposed method of increasing water intake and urine volume is to increase dietary salt (NaCl). However, a study in normal cats fed a diet high in salt for a period of 6 months showed that if there is an effect on urine specific gravity, it is short lived¹⁵. By 3 months, there was no difference between the specific gravity of the control and test diets and this was true at 6 months as well. If the benefit of high sodium diets in controlling recurrence of uroliths is dependent on diluting the urine specific gravity, these results suggest this benefit is transient.

Despite the evidence in short-term studies in healthy cats that increased salt intake appears to be safe, a recent study revealed some negative consequences of feeding high salt foods to cats¹⁶. 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 renal insufficiency and physiological status over a three month period. In cats with subclinical kidney disease, the high sodium diet resulted in an increased progression of their disease (significantly increase serum creatinine, urea nitrogen and phosphorous), and increased urinary calcium excretion. Why is this important? While chronic kidney disease is more common in older cats, just under 1/3 of cases are 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 diets or feeding increased salt diets to cats. The incidence of calcium oxalate nephroliths are also increasing. Twenty-five percent of cats with chronic renal failure have stones in the upper urinary tract and 70% of stones in the upper urinary tract are calcium oxalate¹⁷. Many over-the-counter foods and some foods designed to manage feline urinary tract disease contain similar levels of salt to this study or higher.

Other safer methods that can be used to increase 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, adding another water bowl ensuring it is shallow and wide (cats don't like their whiskers to touch the sides of the bowl) and the use of water fountains.

The inflammation of FLUTD is associated with "oxidative stress" resulting in increased production of free radicals which contribute to the progression of the disease. FIC in particular, is an inflammatory (neurogenic) condition and stress is a big 'flare' factor. The addition of omega-3 fatty acids to the diet helps with reducing bladder wall inflammation as they are incorporated into all cell

membranes of the body where they exert anti-inflammatory effects¹⁸. Antioxidants such as vitamin E and beta-carotene incorporated into FLUTD diets help protect against free radical production from inflammation. Antioxidants also help protect against calcium oxalate deposition.

Dissolution of Struvite

Three struvite dissolution diets are available in Australia at the time of writing with an average time to dissolution for uroliths ranging from an average of 11 days (Hill's™ Prescription Diet™ s/d Feline), 19-24 days (Royal Canin® Urinary S/O LP34) and 27 days (Hill's™ Prescription Diet™ c/d Multicare Feline). During the dissolution period, it is advised that radiology and urinalysis should be performed every 2 weeks.

Management of Struvite

After dissolution or surgical removal of struvite stones, cats should be transitioned to a struvite management diet formulated with controlled magnesium and phosphorous, avoiding excessive sodium and with a target urinary pH of 6.2-6.4. Diets currently marked to manage struvite include Hill's™ Prescription Diet™ c/d Multicare Feline, Royal Canin® Urinary S/O LP34 and Eukanuba® Veterinary Diets Urinary Struvite Formula. Aiming for 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 fed higher fibre weight management diets such as Hill's™ Prescription Diet™ w/d Feline.

Management of Calcium Oxalate

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. In addition, increased insoluble fibre decreases calcium absorption from the gastrointestinal tract which is useful in cats with idiopathic hypercalcaemia. Diets currently marked to manage calcium oxalate 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 pH 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 pH is too acidic. Urinalysis should also be performed 3 to 6-monthly on a fresh, non-refrigerated urine sample and survey radiographs twice yearly are advised.

Management of Urate

Cats with urate uroliths often have an underlying hepatic or metabolic disorder but frequently it cannot be identified. These cats should be assessed for liver disease and if found they should be fed a liver management diet. If nothing 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 marked to manage urate include Hill's™ Prescription Diet™ k/d and l/d Feline 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 3 to 6 monthly.

Environmental Enrichment and Behavioural Management

Environmental enrichment and behavioural management are critical pieces of the management puzzle and are especially appropriate for decreasing stress in indoor cats with FIC. It is important to provide outlets for typical cat behaviour such as scratching poles and elevated resting perches (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. Provision of a water fountain also encourages play and activity which helps with environmental enrichment. Feeding in a feline Kong® or hiding a portion of the daily food around the house thus creating a 'treasure hunt' can help 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 are beneficial such as using a fishing pole with feathers on the end. Placing cardboard boxes and paper bags around the house encourage cats to explore, play and hide in.

Litter box management is an essential component of overall management 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-story home there should be at least one litter box on each floor. Litter boxes should be accessible and with at least two exit points avoiding dead ends and they should be placed away from noisy appliances and dogs. Use of clean, clumping clay-based litter is preferred by cats. Clean the litter boxes at least once a day and thoroughly once per month. Cats who have suffered pain and

discomfort urinating may associate this with the litter box and thus subsequently develop litter box aversions and hence periuria. It is important not to punish periuria as this just adds to the stress. To address this problem, the 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 have a positive impact.

Pharmacological

Pharmacological treatments such as analgesics, facial pheromone and glycosaminoglycans (GAGS) have also been used to manage FLUTD. Feline synthetic facial pheromone (Feliway®) has been shown to improve grooming and food intake which are indicators of decreasing stress¹⁹. One hypothesis for the development of FIC is that there is damage to the glycosaminoglycan (GAGs) layer lining the bladder. Glucosamine is an important intermediate for the formation of GAGS, however, no significant difference in the number of days with cystitis clinical signs was found in a study where 40 cats with spontaneous non-obstructive FLUTD were given 125mg glucosamine/day PO or placebo²⁰.

Summary

Feline lower urinary tract disease can have a big impact on the family-cat bond and affects the quality of life of cats and their owners. Nutrition, environmental enrichment and behavioural management are important components of the multimodal management of cats with FLUTD.

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