FELINE LOWER URINARY TRACT DISEASE

Dr Andrew H. Sparkes BVetMed PhD DipECVIM MRCVS

The Feline Unit
Centre for Small Animal Studies
Animal Health Trust
UK
Andy.sparkes@dsl.pipex.com

A spectrum of disease

Feline lower urinary tract disease (FLUTD) is a spectrum of different diseases that present with a common set of clinical signs irrespective of the underlying cause – these include dysuria, haematuria, pollakiuria and periuria and behavioural changes such as aggression and perineal overgrooming. Additionally male cats may develop stranguria with urethral blockage which, if left untreated, will result in acute renal failure within 1-3 days.

Despite the common array of clinical signs exhibited, there are a number of potential underlying aetiologies for FLUTD which have to be considered and achieving a definitive diagnosis requires a logical and structured approach to the investigation of cases.

In general, idiopathic cystitis accounts for 50-70% of cases of FLUTD and is universally the most common diagnosis made. Urolithiasis and urethral obstruction (which can be caused by a single urolith, an accumulation of small uroliths, a urethral plug, urethral stricture, or functional spasm of the urethral sphincter) are also common causes of disease, together accounting for up to 40% of clinical cases.

Bacterial cystitis

While most surveys suggest bacterial cystitis is rare in cats (<2-3% of cases of FLUTD) and while it is undoubtedly vastly less common than in dogs, the low prevalence in some studies may reflect biases seen in referral populations. Some studies suggest that up to 10% (or possibly more) of first-opinion cases may have bacterial cystitis. Routine sediment analysis of a urine sample collected by cystocentesis is extremely valuable, and in most cases of bacterial cystitis this will reveal clear evidence of its presence (pyuria, bacteriuria). Where evident, or where there is any doubt, bacterial culture can confirm the diagnosis and allows selection of the most appropriate antibiotic. Intereference with innate defence mechanisms (eg, repeat catheterisation and perineal urethrostomies) are known to increase the risk of bacterial cystitis and this is also much more common in older cats due to ageing cats tending to produce less concentrated urine and thus having a microenvironment where bacterial growth is more likely to occur.

Urolithiasis

Calcium oxalate and struvite uroliths occur with approximately equal frequency in cats and together account for around 90% of all uroliths. While struvite stones can be dissolved with appropriate dietary management, oxalate cannot and require surgical removal. There is a significant risk of recurrent urolithiasis in any individual that has experienced one episode, so taking measures to help prevent their recurrence provides good preventative healthcare. Long-term prevention of recurrence depends on modifying the urine composition to reduce the risk of further crystalluria and stone formation.

Some of the known risk factors for oxalate and struvite urolithiasis are effectively at odds with each other (such as urine pH, and urine magnesium concentration), and thus diets designed to address the specific requirements for prevention of these two different types of stone are ideal for maintenance in these cases. Wherever possible the use of tinned/sachet foods rather than dry foods is recommended to help produce less concentrated urine.

Urethral plugs and crystalluria

Urethral plugs are possibly the single most common cause of urethral obstruction in cats, but their underlying cause remains uncertain. Most plugs have a high matrix content (>50%) of within which crystalline material, cells and cellular debris becomes trapped. Together, these components form the urethral obstruction. Although the matrix is composed largely of proteinaceous material, its source has not been

determined. However, it is likely that in at least a proportion of these cases, the underlying cause is idiopathic cystitis, with the bladder inflammation contributing to increased secretion and/or leakage of various proteins into the urine. In the vast majority of cases, the crystalline component of urethral plugs is struvite. The finding of struvite crystalluria (and some other forms of crystalluria) is not of itself an abnormality. Many healthy cats (and indeed other animals!) produce crystalluria, but its presence does suggest that the urine is supersaturated with the crystalloid materials, and this would be one risk factor for urolith development. It is not necessarily appropriate to modify the diet of healthy individuals producing crystalluria, but in a cat that has previously had an episode of urolithiasis, urine should be monitored to ensure dietary modification has been successful in understurating the urine (ie, crystals should be absent). Also in cats that have experienced urethral plugs, the diet should be modified to undersaturate the urine with magnesium, ammonium, and phosphate, and thus at least eliminate the crystalloid component that may contribute to repeat plug formation. In this situation, although crystalluria is not the cause of the disease, it does contribute to the formation of a plug that cannot be passed through the urethra. Thus dietary modification to eliminate struvite crystalluria may help prevent recurrence.

Urethral spasm

Not just with urethral plugs, but in many other forms of FLUTD, the disease may not be confined to the bladder but may also involve inflammation of the urethra. This may also be exacerbated by iatrogenic damage to the urethra or irritation of the urethra with the use of indwelling catheters. Such inflammation may result in significant urethral sphincter spasm, and there is good evidence that in some cats this is severe enough to mimic physical urethral obstruction. Where urethral spasm is suspected a combination of smooth and striated muscle relaxants should be used to relax both the internal and external sphincter muscles. Common recommendations are to use either dantrolene (2-10 mg/cat PO tid) or diazepam (2-5mg/cat PO bid/tid) together with either prazosin (0.5 mg/cat sid-bid) or phenoxybenzamine (2.5-7.5 mg/cat sid/bid).

Idiopathic cystitis

Idiopathic cystitis is a diagnosis that can only be made by exclusion of known causes of FLUTD, and thus following a logical diagnostic work-up (see Table 2). The majority of cases of idiopathic FLUTD (iFLUTD) spontaneously resolve within a few days irrespective of therapy, making response to treatment very hard to assess. Often, what is taken to be improvement due to therapy is in fact simply spontaneous recovery. A plethora of drugs are used to treat iFLUTD, many of which have not been the subject of any clinical trials, and of the few published well-controlled studies, regrettably no interventional medical therapy has been shown to be of significant benefit in these cases.

Nevertheless, a number of drugs have only been evaluated in short-term studies (lasting 1-2 weeks) of idiopathic cystitis, and the fact that drugs such as prednisolone and amitriptyline are not significantly different from placebo therapy in this situation may simply reflect the rapidly self-resolving nature of this disease. Of more clinical value is the use of long-term placebo controlled studies looking at frequency and severity of recurrent episodes, but such studies are less common as they are more difficult and more expensive to conduct.

The importance of diet in idiopathic cystitis

Although the use of diets to specifically to minimise production of urinary crystals has little or no scientific rationale in the management of iFLUTD, dietary manipulation is the single most important component of long-term management of this disease.

Dietary change is the only form of therapy that has consistently been shown to be of real benefit in cases of iFLUTD. Based on our current knowledge, this forms the most important part of long-term management. Several studies have now confirmed the results of an earlier investigation that showed cats fed a wet (tinned) diet had a much lower rate of recurrent signs of idiopathic cystitis than those fed a dry diet. The urine concentration produced in response to feeding the wet diet was much lower than that of the cats fed the dry diet, and it is thought that producing more dilute urine (and presumably thus also encouraging more frequent urination) are major mechanisms of the observed benefit. Feeding a wet (tinned/sachet) diet rather than a dry diet is thus always recommended for iFLUTD, and the feeding of a 'pH neutral' diet (a urine pH in the region of 6.3 is typically found in cats on a 'natural' diet of rodents) that will avoid extremes of urinary pH is also likely to be of benefit. The use of a relatively low solute-load diet helps in the production low urine concentration, and this is preferable to trying to encourage greater urine production through the addition of salt to the diet. The latter could be associated with a number of potential adverse effects such as volume expansion and contributing to hypertension, and exacerbating any renal compromise present. Encouraging

water intake without salt supplementation is thus preferred and the use of 'pet fountains', flavoured waters and other methods of enhancing water intake (beyond just the use of wet diets) also has a good role to play. In cases of recurrent iFLUTD, a primary aim should be to reduce the urine SG to 1.035 or less, and avoid abnormal acidification or alkalinisation.

Drug therapy in idiopathic cystitis

Recent evidence from investigation of iFLUTD cases has revealed a number of similarities to interstitial cystitis in humans. Although differences also exist there are certainly many striking similarities. There is evidence from careful studies that both conditions may be associated with decreased urinary excretion of glycosaminoglycans, an increased bladder wall permeability, and increased circulating catecholamine levels (although paradoxically relatively low cortisol levels and blunted cortisol responses to ACTH). On the basis of the similarity between these two conditions, some of the treatments that have been shown to be useful for the management of interstitial cystitis in humans have been tried in cats with iFLUTD.

Glycosaminoglycan (GAG) replacers (e.g. pentosan polysulphate, glucosmaine) fall into this category and are now commonly used in cats with iFLUTD. Although the finding of significantly reduced GAG concentrations in the urine of affected cats provides a good rationale for their use, clinical experience with these drugs has been variable. In two long-term controlled studies, GAG replacers did not appear to make a significant difference overall to the recurrence of iFLUTD in affected cats. Nevertheless, of interest is that both these studies identified some individual cats that did seemed to consistently respond to GAG-replacer use, and have recurrent signs when therapy was stopped. Although still uncertain, it seems that some cats may genuinely benefit from this therapy, although possibly not most. On this basis, trial therapy is certainly warranted in refractory cases.

Amitriptyline has also been used to treat interstitial cystitis in humans. Being a tricyclic antidepressant drug, it certainly has some central nervous system effects which may help in controlling iFLUTD, especially as stress factors appear to be involved in at least some cats. However, the drug has a number of other potential beneficial effects in terms of reducing neurogenic inflammation in the bladder and controlling the discomfort associated with the disease. Generally, amitriptyline has been used at a dose of 2.5-10 mg per cat, given once daily in the evening (as administration may cause temporary sedation). Although short-term studies have not been able to demonstrate a benefit, one long-term open uncontrolled study did suggest genuine benefit in some cats with long-standing intractable cystitis. Again, in severe, intractable cases this drug is worth considering.

Consideration should also be given to environmental factors and potential stress factors that could impact on affected cats. Inter-cat aggression and dominance may be an important trigger factor in some and the use of environmental enrichment/modification together with feline pheromone sprays/diffusers could also be a consideration in some situations.