A multimodal approach to feline and canine cystitis management

Author: Kit Sturgess

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Inflammation of the bladder wall, known as cystitis, is a common presentation in cats and dogs and has the following typical characteristics:

- Stranguria – difficulty in micturition, in which the urine is passed only drop by drop with pain and tenesmus.
- Pollakiuria – increased urinary frequency.
- Periuria – inappropriate urination.
- Haematuria – which may be microscopic.

![Figure 1. Approach to management of FLUTD.](image)

Not all patients will show every clinical sign listed. Rarely, patients will have cystitis with no outward clinical signs – these cases are most commonly bacterial associated with polyuria/polydipsia and endocrine disease, such as diabetes mellitus or hyperadrenocorticism.

The key differential to this pattern of clinical signs is urinary tract obstruction. As obstruction is a life-threatening condition, it should always be excluded before treating a patient as a cystitis case. Typically, obstructed patients will have large bladders that can be palpated or imaged with ultrasound.

Cystitis patients tend to have small bladders and may show pain/discomfort on palpation of the caudal abdomen. In chronic cases, the bladder wall may feel small, thickened and irregular, with palpation causing reflex attempts to micturate. Excessive grooming and staining of the hair around
the vulva/prepuce may also be noted. Clinical history is important, in particular, to try to distinguish cystitis from incontinence or behavioural disease leading to periuria.

Optimal treatment in cystitis cases is centred on identifying and treating the underlying cause. Differential diagnoses are listed in Panel 1. Depending on the clinical signs and patient wellness, a first episode may be managed symptomatically without investigation; although, if available, dipstick and urine specific gravity (USG) analysis of a free catch urine can be inexpensive and helpful in excluding some underlying causes, such as diabetes mellitus.

![Image of ultrasound](image.png)

**Figure 2.** Effect of an empty bladder on wall thickness and layering.

Particularly where costs are an issue and tests need to be carefully selected, urinary tract infection is uncommon when the urine is concentrated above 1.035 to 1.040 and acidic. It should be noted crystalluria is a very rare cause of cystitis (Bell and Lulich, 2015).

A general approach to the investigation of cystitis cases in cats is illustrated in Figure 1, with ultrasound and bacterial culture (preferably on a cystocentesis sample) being the two highest-yield and least-invasive options.

Both tests can be problematic in some cystitis cases (especially cats) where the bladder is virtually empty, and assessing wall thickness and layering can be problematic due to the thickening and irregularity of the mucosal surface that tends to be present in a poorly filled bladder (Figure 2).

**Canine cystitis**
Table 1. Causes of FLUTD.

Little data are available for dogs and idiopathic cystitis is not a well-described condition; most dogs with cystitis have a defined underlying cause, with infection and urolithiasis being most common.

On occasions, chronic inflammation (without clear evidence of infection) can occur and lead to polypoid cystitis (Figure 3; Martinez et al, 2003; Díaz Espiñeira et al, 1998) or mucoid cystitis (Figure 4).

Prostatitis can present with clinical signs that are very similar to cystitis (haematuria, stranguria), making rectal examination (with care as prostatitis can be very painful) an important part of the physical examination in dogs presenting with cystitis-like signs.

In dogs, stranguria or pollakiuria are more likely to reflect urethral or neurogenic disease than idiopathic cystitis. Diagnosis can be difficult in the absence of urethral pressure profilometry and cystometry, which have extremely limited availability.

**Idiopathic detrusor-urethral dyssynergia**

Idiopathic detrusor-urethral dyssynergia is characterised by a normal initial stream that is quickly attenuated, stop-start urination or frequent unsuccessful posturing to urinate without straining (Díaz Espiñeira et al, 1998). Prazosin, an α1-selective adrenergic antagonist at 1mg/15kg every 8 to 12 hours, is effective in inducing urethral smooth muscle relaxation in the majority of cases.
Panel 1. Differential diagnosis of cystitis-like signs.

Prazosin can cause significant hypotension – particularly on initiation of treatment – and this drug should be used with care in cases with known or possible occult heart disease; other drugs should be considered, such as propantheline or oxybutynin.

**Detrusor instability**

Detrusor instability results in detrusor contraction during storage, or where there is low compliance of the detrusor present clinically as pollakiuria with or without incontinence (Nickel et al, 1999). Decreased detrusor compliance also occurs secondary to inflammation and this is usually termed urge incontinence. Treatment is with anticholinergic medication; the author uses oxybutynin at 0.2mg/kg by mouth every 8 to 12 hours. Side effects are rare, but include diarrhoea, constipation, urinary retention, hypersalivation and sedation.

**Urethritis**

Urethritis will tend to cause stranguria and pollakiuria in dogs, with granulomatous urethritis being most commonly reported. Diagnosis usually requires biopsy either endoscopically or surgically.

**Feline cystitis**

Far greater information is available on idiopathic FLUTD (feline idiopathic cystitis; FIC), but overall studies have generally failed to show any of the commonly used treatments, apart from diet, to be
efficacious. A synopsis of the frequency of reported causes of FLUTD in cats is presented in Table 1.

In cats with recurrent episodes of idiopathic FLUTD, careful history taking is important, with detailed information on the lifestyle of the cat, including number of cats in the household, indoor/outdoor, access to water and food, access to places to urinate – litter trays in the house and ease of urination outside (for example, aggressive neighbourhood cat limiting access).

In this respect, an owner diary can be useful to document duration, severity and frequency of episodes and environmental and household conditions around the time of an episode. Frequency and duration of episodes is also valuable in assessing true response to treatment. An effective management strategy in idiopathic FLUTD should at least halve the frequency and/or duration/severity of episodes.

Assessment of a response is further complicated as a strong placebo effect with treatment has been documented that may be as high as 65% – that is, 65% of any apparent treatment effect is due to the act of giving treatment, rather than the treatment itself.

**Dietary recommendations**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Classification</th>
<th>Dose (mg/kg)</th>
<th>Action</th>
<th>Side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenobarbital</td>
<td>α-adrenergic antagonist</td>
<td>2.5 mg/kg to 7.5 mg/kg by mouth every 1 to 2 hours</td>
<td>Decreases smooth muscle tone</td>
<td>Hypersalivation and gastrointestinal tract irritation – side effect rates may be higher than with pranxine</td>
</tr>
<tr>
<td>Phenoxybenzamine</td>
<td>α-adrenergic antagonist</td>
<td>0.1 mg/kg to 1 mg/kg by mouth every 2 to 6 hours</td>
<td>Decreases smooth muscle tone</td>
<td>Hypersalivation – use with care if there is a risk of occult cardiomyopathy</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>Corticosteroid</td>
<td>0.1 mg/kg to 0.5 mg/kg by mouth every 12 hours</td>
<td>Decreases smooth muscle tone</td>
<td>Sedation, increased appetite, paroxysmal excitement and new hyperactivity</td>
</tr>
<tr>
<td>Omeprazole</td>
<td>Proton pump inhibitor</td>
<td>0.05 mg/kg to 0.1 mg/kg by mouth every 8 hours</td>
<td>Decreases smooth muscle tone</td>
<td>Sedation, weakness, constipation, diarrhoea, gastric ulcers, hepatic disease</td>
</tr>
</tbody>
</table>

**Table 2.** Suggested drugs and dose rates of antispasmodics for use in cats with idiopathic FLUTD.

Diets that encourage large volumes of dilute urine (wet diets) have been shown to decrease the recurrence of episodes (11% of cats on wet diets versus 39% of cats on dry diets). No convincing evidence exists that diet type – for example, acidifying diets – has any significant effect and, in some situations, may predispose cats to other problems.

Cats that will only eat dry diets should have water mixed in with the food (if they will accept this) or be provided with a ready supply of fresh water, optimising water availability – for example, fountains versus still water can be helpful. The aim is to try to reduce USG towards 1.030, but even modest reductions in USG seem beneficial.

Studies have also suggested reducing USG not only increases urine volume, but also increases the frequency of urination. Increasing salt levels in the diet will promote thirst and water turnover. Hypertension, secondary to salt-supplemented, does not seem to be a significant issue, but no data exist on the influence of higher salt diets on idiopathic FLUTD.
Therapeutic urinary food

Nutritional factors that may impact expression of lower urinary tract signs, and help manage idiopathic FLUTD and reduce the likelihood of urethral plug formation, include the following:

- Decreasing urine concentrations of pro-inflammatory mediators and crystallogenic minerals.
- Decreasing retention of crystals in the urinary tract.
- Increasing urine concentrations of anti-inflammatory/pro-resolving mediators and crystallization inhibitors.
- Increasing solubility of crystalloids in urine.

![Figure 3. Cystoscopy in a dog with polypoid cystitis.](image)

Long-chain \( \theta \) fatty acids, including eicosapentaenoic acid and docosahexaenoic acid, and antioxidants such as vitamin E, are potent anti-inflammatory agents. Effects of \( \theta \) fatty acids alone have not been evaluated in cats with lower urinary tract disorders; however, they seem to have beneficial urinary effects in studies of other species.

The optimal therapeutic dose of \( \theta \) fatty acids and antioxidants for cats with idiopathic FLUTD have not been determined; a study supports the long-term use of a multi-purpose therapeutic urinary food with enhanced concentrations of these nutrients (Kruger et al, 2015).

Glycosaminoglycans

The urothelium is not innately resistant to the potential corrosive effects of urine. Like the stomach, it is protected by a hydrophobic glycocalyx layer composed of hydrated glycoproteins and glycosaminoglycans (GAGs). GAGs also serve to minimise the adherence of microorganisms and
crystals to the urothelium.

It has long been hypothesised defects in the glycocalyx is a causative factor in the pathogenesis of FLUTD and its restoration a potential therapeutic option. Although some older evidence exists in man that GAG supplementation reduces the severity of symptoms (not supported by most recent publications), similar evidence is lacking in the management of idiopathic FLUTD.

Several low-powered studies have been conducted looking at the benefits of GAG supplementation in the management of idiopathic FLUTD, but none have shown clear benefit, although some indication existed of a trend towards better outcome.

As previously discussed, a multimodality approach to management of idiopathic FLUTD is likely to be necessary and, hence, individual interventions may have a relatively small, but significant, effect. To demonstrate these effects, large (thousands of cats) randomised trials are required.

Figure 4. Urine from a dog with mucoid cystitis.
Parenteral and oral GAG supplements are available. In severe cases, initial parenteral treatment can be followed with oral maintenance. As with all nutraceuticals, it is important manufacturing and quality control occurs to ensure finished products contain the expected amount of active ingredient in the correct isomeric conformation. Pentosan polysulphate 3mg/kg SC day 1, 2, 5, 10 and then every 5 to 10 days thereafter.

A variety of capsule preparations are available that contain glucosamine for use in managing cats with FLUTD. Preparations containing glucosamine for use in the management of osteoarthritis have not been optimised for management of idiopathic FLUTD and are, therefore, not recommended. Other supplements are available, such as a liquid GAG supplement that is supposedly roast meat flavoured.

**Supplements and therapeutic foods**

L-tryptophan, a precursor for serotonin synthesis, has been evaluated as a method of managing stress-related behaviours in cats in a single, two-month, blinded placebo-controlled study (Pereira et al, 2010). This study suggested L-tryptophan supplementation changed the frequency of stress-related behaviours, decreasing signs of anxiety.

A multicentre (placebo-controlled, blinded) study (Beata et al, 2007) evaluated the anxiolytic effects of ?-casozepine in 34 cats. At the end of the study, 10 of the 14 cats judged to have a successful outcome were from the ?-casozepine group. Specific support for the use of ?-casozepine in idiopathic FLUTD is lacking and daily administration of oral medications may be stressful for some cats; however, ?-casozepine can also be delivered in therapeutic foods. Suggested dose rate ?-casozepine (less than 5kg – 75mg/cat by mouth every 24 hours; greater than 5kg –150mg/cat by mouth every 24 hours). All treatments are palliative.

**Medical treatment**

**Amitriptyline (tablets/syrup)**

Amitriptyline 2.5mg/cat to 10mg/cat by mouth once daily is best given in the evenings (if the cat is kept indoors at night) as it may cause mild sedation.

Amitriptyline has been widely used in the management of idiopathic FLUTD – two short-term studies (Kraijer et al, 2003; Kruger et al, 2003) have not shown a positive benefit and one suggested episodes are worsened. One longer-term study (Chew et al, 1998) over one year indicated possible improvement.

Amitriptyline is a tricyclic antidepressant with anti-inflammatory, analgesic, anticholinergic and anti-?-adrenergic properties. It is thought to work by decreasing “stress”, stabilising mast cells, reducing degranulation and reducing histamine release.
Most commonly encountered side effects include dose-dependent sedation, urinary retention (due to anticholinergic activity) and elevated liver enzymes. Liver function should be evaluated on initiation of treatment, one month into therapy and periodically thereafter. Although not licensed for use in animals, amitriptyline appears a safe drug for use in cats, but, in some cases, does require daily, long-term use.

Although amitriptyline will produce rapid relief in clinical signs, this is unlikely to be due to its antidepressant action. For some cats, therefore, intermittent use is effective. If the drug is acting as a tricyclic antidepressant, it takes weeks to months to achieve full efficacy. Reasonable time needs to be given before assessing efficacy of amitriptyline therapy in some cats and needs to be based on good client record keeping.

**Analgesia**

The use of NSAIDs is variably successful, often most effective given very early in an episode, and requires clients to have medication available at home. In severely affected cats, opioids may be required.

**Antispasmodics**

Following an episode of urinary obstruction or idiopathic FLUTD, some cats appear to have difficulty urinating due to urethral spasm or reflex dyssynergia. Similarly, pollakiuria is presumed to be the result of inflammation-induced stimulation of the bladder sacral sensory afferent nerves. Various drugs have been suggested, aimed at improving urethral smooth muscle relaxation.

A study looking at urodynamics of idiopathic FLUTD cats concluded a rationale for using ?1-adrenoreceptor antagonists and skeletal muscle relaxants (Table 2). Limited evidence exists that prazosin may be a better ?-adrenergic antagonist than phenoxybenzamine in cats.

**Corticosteroids**
In acute cases, corticosteroids may control inflammation and stabilise mast cells. A single, small scale, randomised trial using prednisolone for 10 days in the management of idiopathic FLUTD has been published that showed no benefit over placebo in reducing the duration or severity of clinical signs (Osborne et al, 1996). No evidence exists that long-term use is effective and associated side effects need to be considered.

**Maropitant**

Maropitant has Neurokinin one (NK1)-antagonistic activity and is reported to be anti-inflammatory. NK-1 receptors antagonism also has reported anxiolytic and antidepressant effects in man. Maropitant is being used by a number of clinicians in the management of idiopathic FLUTD as, with most treatments, a lack of clear evidence of efficacy exists.

**Intravesicular treatments**

A variety of intravesicular treatments have been considered and used in cats, including lidocaine and sodium bicarbonate, but no evidence exists to date that they have a beneficial effect in reducing severity of signs or recurrence rates. Some solutions, such as Walpole’s (sodium acetate/acetic acid), may serve to worsen pre-existing urethral inflammation.

**Behavioural modification**
Increasing evidence suggests an important role for psychoneuroendocrine dysfunction in cats with idiopathic FLUTD, with chronic stress being a major exacerbating cause. When managing cats with idiopathic FLUTD, it is, therefore, vital time is taken to understand the patient’s home environment.

In that respect, a suitable questionnaire and the input of a behaviourist, in some cases, is appropriate. This has led to development of a multimodal environmental modification approach that has shown recurrence rates in a relatively small uncontrolled study. For cats with recurrent idiopathic FLUTD, prophylactic treatment may be worth considering when stressful events are likely to occur.

It is important to understand a patient’s urination patterns (location, environmental triggers and inappropriate defecation) and distinguish periuria from marking. Attention should also be given to environmental enrichment, as this will likely increase frequency of urination, as well as manage impact on obesity. Other environmental stressors – particularly inter-cat interactions in and outside the household – should be identified and reduced as much as possible.

**Behavioural-modifying drugs**

A variety of drugs have been used in more severe cases while behavioural and environmental modification has a chance to become effective. Evidence to support their use is lacking.

- **Clomipramine** – 0.25mg/kg to 0.5mg/kg by mouth every 24 hours.
- **Buspirone** – 2.5mg/kg to 5mg/cat by mouth every 24 hours.
- **Fluoxetine** – 1mg/kg by mouth every 24 hours.
- **Feline facial pheromones (FFP)** – a lack of evidence exists to support general use of FFP in idiopathic FLUTD, but benefit may exist in some cases, particularly where history suggests a potential conflict exists in a multi-cat household.

Litter trays should be made as comfortable and appealing as possible to encourage frequent use, and one more litter tray provided than there are cats in the household. For cats that urinate outside, while their ability to “hold on” is legendary, efforts should be made to allow frequent outside access.

Urination/defecation outside is a vulnerable time for many cats and nervous cats may be going out, but rarely passing urine. In these circumstances, introducing a safe outside area or indoor litter trays may be worthwhile.

**Perineal urethrostomy**

In a few cats with recurrent idiopathic FLUTD, perineal urethrostomy may be a consideration in an attempt to reduce recurrence rate and aid management.
In a long-term follow-up study of 86 cats (Ruda and Heiene, 2012), the median survival time for all cats was 3.5 years after surgery – 5 cats did not survive the first 14 days after perineal urethrostomy surgery and another 6 cats did not survive 6 months.

Of cats surviving longer than 6 months, 45 (60%) were asymptomatic after surgery and 11% experienced severe signs of recurrent FLUTD. A total of 88% of the owners categorised their cats’ long-term quality of life as good.

Conclusions

Apart from dietary modification and therapeutic foods, a lack of convincing evidence exists that any specific strategy is effective in managing idiopathic cystitis. This is not because other effective strategies do not exist, but reflects the fact idiopathic cystitis is a complex disease and studies to date lack the power required to demonstrate benefit in a condition in which a strong placebo effect exists.

Management is, therefore, best based on a graded approach, guided by circumstances and presentation of an individual case, and supported by owner observation and recording of changes in frequency, severity and duration of episodes. A general suggested progression of intervention is highlighted in Figure 5.

- Use of some drugs in this article is under the cascade.

References


• Pereira GG, Fragoso S and Pires E (2010). Effect of dietary intake of L-tryptophan supplementation on multihoused cats presenting stress-related behaviours, BSAVA.