Feline lower urinary tract disease (FLUTD)

Feline lower urinary tract disease (FLUTD) describes a collection of conditions that can affect the bladder and/or urethra of cats. Unfortunately, the clinical signs are rarely indicative of a particular disease. While there are many conditions that can result in signs of FLUTD (see below) the vast majority of cases are idiopathic (ie. we cannot find the cause).

**Clinical signs of FLUTD**

Cats with FLUTD usually present with signs of difficulty and pain when urinating, increased frequency of urination, blood in the urine, urination outside the litter-box, or even complete obstruction to urine outflow. Some cats show only behavioural change, loss of litter-box training and/or aggression.

The annual incidence of FLUTD in British cats is believed to be around 1 per cent. While the condition can be seen in cats of any age, it is most frequently seen in middle-aged, over-weight cats, which take little exercise, use an indoor litter-box, have restricted access outside and eat a dry diet. Persian cats appear to be predisposed. FLUTD occurs equally in male and female cats; however, neutered cats are more susceptible, and the risk of urinary tract obstruction is greatest in males.

**Causes of FLUTD**

**Causes of non - obstructive FLUTD**

- Non - obstructive idiopathic cystitis 65%
- Bladder stones 15%
- Anatomical defects/cancer/other 10%
- Behavioral problems <10%
- Bacterial infection < 2%

**Causes of obstructive FLUTD**

- Obstructive idiopathic cystitis 29%
- Urethral plug 59%
- Bladder stones 10%
- Bladder stones + bacterial infection 2%

**1. Feline idiopathic cystitis (FIC)**

In the majority of cases of FLUTD no underlying cause can be found. However, while research over the last 30 years has failed to find a consistent cause, a recent hypothesis has suggested that FIC may result from alterations in the interaction between the nerve supply, the protective (glycosaminoglycan [GAG]) layer that lines the bladder, and the urine (see Figure 1.).
FLUTD

Figure 1. Diagram showing how the nervous system may be able to induce/exacerbate inflammation in FIC (neurogenic inflammation)

It is now known that certain nerves within the bladder can be stimulated, either by the brain (in response to 'stress'), or by local triggers within the bladder (e.g., inflammation, bladder stones, concentrated urine, infection, etc.). Regardless of how these nerves are stimulated they release certain neurotransmitters, which can then act to induce and/or exacerbate local pain and inflammation. Where inflammation is triggered by the nervous system it is termed neurogenic inflammation.

A thin layer of protective mucus lines the inside of the bladder. This layer helps to prevent bacteria and crystals from sticking to the bladder wall. It has been suggested that defects in this protective layer may result in increased bladder wall permeability, allowing noxious substances within the urine to cause inflammation. It has been shown that some cats with FIC have reduced levels of GAG within this protective layer. While it is not known whether or not the defect is actually caused by the inflammation, its presence is believed to exacerbate it.

2. Bladder stones
Bladder stones (uroliths) can vary in their composition, with struvite and oxalate forms being most common in cats. Over the last few years the pet food companies have focused on designing diets that help to dissolve struvite stones. Unfortunately, while this has resulted in a decline in the incidence of struvite stones there has been an increase in oxalate stones. Unfortunately, oxalate uroliths are not dissolvable in cat urine, and so must be removed surgically.

3. Urethral plugs
Urethral plugs are of particular importance because they can cause urethral obstruction. They are composed of varying combinations of a protein matrix (various proteins and cells from the bladder and blood) and crystalline material (most typically struvite). The protein matrix is believed to 'leak' from the bladder wall as a result of inflammation. The cause of this inflammation may be neurogenic, idiopathic, or secondary to infection, cancer or bladder stones. Thick protein matrix may cause urethral obstruction without evidence of crystalluria (crystals in the urine). However, where crystalluria is also present, the crystals may become trapped within the matrix, and add to the obstruction. It is therefore the protein matrix that is of primary importance, rather than the presence of crystals per se.

4. Infectious causes
So far, no bacterial, fungal or viral organisms have been consistently shown to cause FLUTD. However, it is still possible that an organism that is very difficult to grow could be involved. Bacterial infection is a very rare cause of FLUTD. Where it is seen, it is usually secondary to
veterinary intervention, bladder stones, an anatomical defect, or cancer. Older cats, particularly those with renal failure, have an increased risk of bacterial infection. However, FLUTD is rarely seen in cats of this age-group.

5. Unifying hypothesis

The different causes of FLUTD may occur individually, or in various interacting combinations (Figure 2). For example, the formation of urethral plugs may result from concurrent, but not necessarily related, disorders, ie the simultaneous occurrence of urinary tract inflammation and crystalluria. While obstruction most typically results from the formation of urethral plugs, it may also be caused by the passage of small bladder stones, or from pain-induced urethral spasm. Although, inflammation without crystalluria can result in obstruction with protein matrix, it more typically causes bloodstained urine and signs of pain when urinating. While crystalluria is often clinically silent, if persistent, it may predispose to the development of bladder stones, and these, in turn can lead to urethral obstruction, and bladder inflammation.

![Figure 2. Flow diagram illustrating how interaction between urinary tract inflammation and urine crystals can lead to different clinical presentations.](image)

* Urinary tract inflammation may be neurogenic (triggered via the nervous system), idiopathic (cause unknown), or secondary to infection, cancer or bladder stones.

**Diagnosis**

Diagnosis of FIC is made by exclusion of all other causes of FLUTD. A practical, step-wise, approach is used. It often includes taking blood samples to rule out systemic disease, followed by collection of a urine sample. The urine will be assessed for its concentration (specific gravity), and for the presence of crystals, protein, red and white blood cells, and bacteria (infection). Taking abdominal radiographs, performing contrast bladder studies, and/or ultrasound examination of the bladder may then be performed.

If no physical cause can be found it may be thought to be a purely behavioral problem. However, if the cat is not currently showing signs of FLUTD repeating the investigation when the cat is showing signs may reveal more obvious disease. It is interesting to note that many cats which are believed to have a purely behavioral problem have a history of FLUTD at some time in their past.

**Management of FIC**

Most cases of non-obstructive FLUTD are self-limiting; usually resolving within five to 10 days. However, most affected cats have episodes of clinical signs, which recur with variable frequency. The recurrent episodes generally tend to decrease in frequency and severity over time. Despite the likelihood of spontaneous resolution, treatment is recommended for a number of reasons:

- FIC is very painful and distressing to the cat.
- Cats with FIC may self-traumatise their perineal region (the area below their tail).
- Cats with FIC may stop eating.
- Male cats with FIC are at risk of developing urethral obstruction, which can be fatal.
- Cats with FIC may develop behavioural changes, become aggressive to their owners or other cats within the household, or may lose their litter-box training.
- Having a cat with FIC is very distressing to the owner.
Unfortunately, few treatments for FLUTD have been investigated by well-controlled experimental studies. Most recommendations are therefore based on uncontrolled clinical observations and personal opinion. Also, since FLUTD is usually self-limiting, many treatments may appear to be effective, when they actually have no positive effect. All treatments should therefore be considered with appropriate caution.

As more drugs are tried, the list of those that are either unhelpful, or even harmful, is growing. Of those treatments that have been critically assessed corticosteroids and certain antibiotics have been shown to have no beneficial effect, except in those rare cases where bacterial infection is present and antibiotics are actually required.

The list of medications and interventions that have been considered for the treatment of FLUTD is far too extensive to be included in this article. The author has therefore chosen to describe her current approach to the management of FIC, which is aimed at addressing the factors that are believed to under the disease; i.e. the nature of the nerve supply into the bladder, the content of the urine, and the protective GAG layer.

**First line of treatment:**

1. **Reduce stress**
   Stress plays a key role in FIC; it has been identified as a ‘flare factor’ that can precipitate a recurrence of clinical signs. Identified stressors include abrupt changes in diet, environment, weather, overcrowding, owner stress, or the addition to the household of new pets or people. Stress associated with urination can be particularly significant, e.g. an unsuitable position or content of the litter box, competition for the litter box, aggressive behaviour by other cats while the cat is trying to use the litter box or when urinating outside, etc.

   It is essential to reduce the level of stress to which the cat may be exposed. Providing a safe, clean area in which the cat can urinate, reducing overcrowding or bullying, and reassuring the cat as much as possible may achieve this.

2. **Alter the content of the urine**
   Altering the diet is the easiest way to modify the urine. Previously, much interest has been placed on changing the acidity, magnesium, and calcium content of the urine. However, it is now believed that the single most important factor is the rate of water turnover. The aim is therefore to increase water turnover and dilute any noxious components within the urine. Rather than altering the content of a dry diet, it makes much more sense to simply feed a wet one! Where significant struvite crystalluria and/or struvite bladder stones are present, feeding an acidified wet diet may be useful.

   **Dietary recommendations:**
   
   - Change diet to canned food or moisten dry food.
   - Supply free access to water and encourage cat to drink.
   - Do not feed acidified diet if urine is acid and struvite uroliths are not a problem.
   - Long-term use of highly acidified diets can be very harmful.

3. **Repair the protective GAG layer**
   In theory, therapy to replace the GAG layer should be beneficial. It relies on the assumption that GAG supplements gain access to the bladder and attach to the defective bladder lining. GAGs may also be of benefit because of analgesic (‘pain killing’) and anti-inflammatory properties. However, while these compounds have shown some positive responses in humans with interstitial cystitis, controlled studies in cats are currently lacking. From human studies, it appears that there are differences in the relative efficiency of different GAGs to produce positive effects, and the same is likely to be true in cats.

   While controlled studies have not yet been performed, the author has been using GAG supplementation, and has generally been pleased with the response. Supplements can be given by mouth or subcutaneous injection.

   Supplementation can begin with a higher dose at the time of initial presentation and then be reduced to a maintenance level. For those cats where oral supplementation is not possible, and repeated visits to the veterinary practice cause distress, injectable ‘Cartrophen’ can be dispensed for home-medicating (in a similar fashion to that usually used for insulin).

   Observant owners may notice that some cats show mild signs before the onset of an episode of...
FIC. The duration of these signs may vary from a few days to a few hours. Signs may include increased grooming of the hind-end, or inter-cat aggression initiated by the FIC sufferer. These signs may relate to increasing pain. The instigation of treatment at this point, or increasing the dose of medication at this time, may help to reduce the severity and duration of the episode, or prevent it from occurring altogether. This approach can also be used if a stressful episode is anticipated, (e.g. a visit to the vet, a stay in a cattery, builders in the home, etc.)

Pentosan Polysulphate ('Cartrophen'; Arthropharm Limited) is given by subcutaneous injection. N-Acetyl Glucosamine is a precursor for GAG. It can be given as 'Cystease' (distributed by Ceva), or Cystaid (distributed by VetPlus).

Side effects of GAG supplementation: Prolonged bleeding times, nausea, and diarrhoea. Possibly, insulin resistance.

**Second line of treatment:**

1. **Relief of urethral spasm**
   Where urethral spasm has been shown to be causing a problem specific spasmolytic drugs may be beneficial. They act by causing relaxation of the muscles within the urethra.

2. **Tricyclic antidepressants**
   Tricyclic antidepressants (e.g. Amitriptyline) have been used in some very severe or chronic cases of FLUTD. They have been found to be beneficial in the treatment of humans with interstitial cystitis, and in a number of cats with FIC, however, they should always be used with caution. They act as anti-depressant, and also have direct affects on the bladder where they can increase bladder capacity, and have anti-inflammatory, and 'pain killing' properties.

3. **Analgesia ('pain killers')**
   While some 'pain killers' may reduce the severity of the pain, they are rarely sufficient to significantly reduce the clinical signs of FLUTD.

**Treatment summary**

It is important to note that all current treatments for FLUTD are merely palliative! The best results are gained by instigating a number of changes, ie reducing stress, feeding a wet diet, replacing GAGs and, if necessary, relieving urethral spasm or giving tricyclic antidepressants. In the majority of cases this, when tailored to the individual cat, will reduce or prevent further clinical signs.

This information sheet is produced by the Feline Advisory Bureau

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