Lower urinary tract disorders are common in cats. In previous decades, the focus of study has been on causes and management of crystalluria. As struvite crystalluria was successfully addressed through nutritional changes resulting in urine acidification, the frequency of calcium oxalate crystalluria increased. This encouraged emphasis on urine relative supersaturation (RSS), concentration and a pH neutrality. Nevertheless, cats still present with characteristic lower urinary tract signs (LUTS), namely dysuria, pollakiuria, hematuria, stranguria and periiuria. The cause of approximately 65% of non-obstructive lower urinary tract disease is of unknown despite appropriate diagnostic testing. (Possible causes of LUTS are shown in Figure 1. A diagnostic approach to cats with lower urinary tract signs is shown in Figure 2.) These patients are described as having an idiopathic cystitis (IC). It is likely that this syndrome is multifactorial even within the same cat. The course of human interstitial/idiopathic, including interstitial cystitis, is known to be impacted by stress. There is evidence that there are immunological and neuroendocrine components in our feline IC patients as well.

Studying feline idiopathic cystitis (FIC) is extremely challenging not only because of its multifactorial nature, but also because clinical signs are self-limiting. In approximately 91% of cats, evidence of discomfort resolves within 7 days without treatment. Subsequent episodes are also acute in nature and occur once or twice a year. As cats get older, the frequency and severity of the flare-up decreases. A small number of cats experience chronic persistent disease lasting weeks to months. Inflammation associated with each incident may result in functional or mechanical obstruction. The first may be caused by urethra swelling, spasm, or reflex dyssynergia, while accumulations of inflammatory debris or the formation of matrix plugs can cause mechanical obstruction. Urachal diverticulae are a possible sequelae to FIC.

What causes the inflammation in non-obstructed LUTD? Many studies have attempted to answer this question yet results have been disappointing. Infectious agents, dietary causes (mineral composition, RSS and urine pH), neurogenic, anatomic, traumatic, neoplastic and iatrogenic etiologies are all implicated in some individuals, but the largest category remains idiopathic in origin.

Buffington and colleagues have investigated the problem from another angle asking whether a susceptible individual might develop FIC if they are in a provocative environment. Indeed, similar to the human model of IC, he found that affected cats have structurally altered adrenals, more reactive somatosensory spinal tracts and a larger pontine locus coeruleus (LC, the most important source of norepinephrine in the CNS) This suggests that patients with IC have increased sympathetic nervous system (SNS) activity even during periods without clinical signs. He has reviewed published epidemiologic data regarding the role of environment and its physiologic effects on risk for disease, especially in susceptible individuals. External influences include excessive body condition, decreased activity, being restricted to eliminate in a litter box, being strictly indoors, relocation of home, living with other cats and weather changes. Stressors (internal/perceived influences) that affect different individuals to a greater or lesser degree include an impoverished environment, lack of stimulation, noise, restraint, and lack of control over his/her environment (including meals). The stress response invokes changes in immune, neurologic and vascular status, all of which can cooperatively result in inflammation. With sufficiently severe stress, sensory input and inflammatory mediators stimulate the hypothalamic-pituitary-adrenal axis (HPAA) and the aforementioned pontine LC – norepinephrine
system. With chronic stimulation, over time normal control is lost and affected individuals overreact physiologically to threatening or disruptive situations.

Buffington and co-workers also identified that cats, as humans, with IC frequently have co-morbidities and has called this the Pandora Syndrome. He suggests that the bladder, rather than being the perpetrator of the LUTS, may be a victim of the systemic process associated with the sensitized central stress response system. Comorbid disorders include behavioural, endocrine, dermatological, respiratory, cardiovascular, and gastrointestinal problems. FIC does not necessarily precede the other conditions. In humans, the effects of chronic in utero stress on the health of the offspring are well documented. It may well be that genetic and similar epigenetic events contribute to the susceptibility of an individual making them at risk should they be exposed to provocative events.

**MANAGEMENT OF CATS WITH FIC**

Evaluating the efficacy of therapies for FIC is very difficult because of the waxing-waning nature of the disorder. Stress reduction appears to be a cornerstone for managing cats afflicted with FIC. Addressing environmental needs is essential (not optional) for optimum wellbeing of the cat. Environmental needs include those relating not only to the cat’s physical surroundings (indoors or outdoors; in the home environment or at the veterinary practice) but also those affecting social interaction, including responses to human contact. Cats need to have multiple and separate locations for each resource (food, water, clean litter, toys, stable scratching surfaces, perches and resting areas). The overview of a therapeutic and management approach to a cat with LUTS is shown in Figure 3.

It is essential that cats are able to express their natural behaviours. Cats use olfactory and chemical information to evaluate their surroundings and maximize their sense of security, comfort and feel in control of their surroundings/environment. Depositing pheromones through cheek and paw pad marking as well as urine is key for a cat’s sense of control. In some situations, when a cat is marking with urine, it may be possible to get the cat to make a less offensive mark (from a human perspective). Cheek marking wall corners may be encouraged by using Feliway and not washing the cat’s natural oils off walls and furniture. Likewise, providing secure, stable scratching surface placed in the location being urine marked, may result in the cat scratching and marking in that manner rather than spraying. The AAFP and ISFM Feline Environmental Needs Guidelines is an excellent resource freely available from: (jfm.sagepub.com/content/15/3/219.full.pdf+html).

**Pheromone Use**

Feliway™ is a synthetic analog of a feline facial pheromone that is thought to increase emotional stability. Its use in the reduction of inappropriate urination needs to be studied further. Studies done to date have shown a reduction in urine marking of less than three months duration of over 96%. In cats who had been marking for four months or longer, there was a reduction of marking in 91% of cats after 35 days of environmental treatment. A third study showed that while there was a significant reduction in all households in which Feliway™ was applied, 2/3 of the households still experienced some marking.

The product is sprayed directly on places soiled by the cat and also any prominent vertical locations in the environment. A daily application is necessary until the cat is noted to exhibit facial rubbing on the site. If the cat does not exhibit facial rubbing, then daily application to the environment should be continued for one month. Plug-in diffusers provide a constant, slow release of pheromone covering an area of 500 to 700 square feet (50-70 m²), but must not be covered, placed behind a door or under furniture.
Diet and Drugs
Feeding a diet that produces dilute urine with a neutral pH seems to help cats have fewer recurrences of FIC or any type of lower urinary tract disease. Canned food helps to ensure that the urine is dilute, making it less concentrated (hence, less irritating) and reducing the chance that crystals can form. Having plenty of fresh water available in multiple places in a form the individual cat likes will encourage drinking. Some cats prefer drinking from a recirculating water fountain, others prefer wide bowls. Feeding a diet that has omega-3 fatty acids along with anti-oxidants may also provide beneficial anti-inflammatory effects. Finally, being consistent both in time of feeding as well as diet being fed is very important in reducing stress.

Many drugs have been used to try to reduce the reoccurrence of FIC. Amitriptyline may be helpful in some cats if it is given on an ongoing basis. It is an antidepressant and agent that stabilizes mast cells which may degranulate in some individuals with FIC. Glucosaminoglycans have also been studied and have variable, but generally poor, results. Best results appear to occur with diet, environmental and stress management rather than drug therapy.

SUMMARY
Lower urinary tract disorders are common in cats. Once appropriate diagnostics have ruled out direct causes, for most cases of non-obstructive LUTD, a more global approach needs to be taken, looking at and addressing the role of the cat’s external and internal environments.
Figure 1: Possible causes of lower urinary tract signs in cats with or without co-morbid conditions (Pandora Syndrome) (from Chew D, Buffington CAT, FLUTH Symposium 2014)

Figure 2: Diagnostic approach to cats with lower urinary tract signs (from Chew D, Buffington CAT, FLUTH Symposium 2014)
Figure 3: Algorithm showing a therapeutic and management approach to a cat with lower urinary tract disease
REFERENCES AND FURTHER READING

- Buffington CAT. External and internal influences on disease risk in cats. JAVMA, 220 (7): 994-1002, 2002.