

# Chronic Lower Urinary Tract Signs in Cats

## Current Understanding of Pathophysiology and Management



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### KEYWORDS

- Chronic lower urinary tract signs • Indoor house cats
- Multi-modal environmental modifications • Central threat response system

### KEY POINTS

- Clinical research on cats with cLUTS has identified genetic factors, epigenetic influences, and environmental influences associated with cLUTS.
- Clinicians should take a “global” approach when obtaining a history, performing the physical examination, and considering pertinent diagnostics and therapeutics to manage the clinical signs of their patients.
- We currently perceive FIC to be an “anxiopathy” - pathology resulting from chronic activation of the central threat response system (CTRS).
- Early intervention with MEMO could help prevent an initial episode, or to prevent a single episode from progressing to a chronic disease.

### INTRODUCTION

This article is dedicated to the memory of Dr Carl Osborne, who in 1984 suggested that, “the term feline urologic syndrome be substituted with descriptive terms pertaining to the site (urethra, bladder, and so on), causes (bacteria, parasites, neoplasms, metabolic disturbances, idiopathic forms, and so on), morphologic changes (inflammation, neoplasia, and so on), and pathophysiologic mechanisms (obstructive uropathy, reflex dyssynergia and so on) whenever possible.”<sup>1</sup> Unfortunately this advice was not implemented, and the name feline lower urinary tract disease (FLUTD)

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Funding provided for many of the studies mentioned in this article are from the NIDDK and Maddie’s Fund; National Center for Advancing Translational Sciences, National Institutes of Health, through grant number UL1 TR001860 and linked award TL1 TR001861.

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Vet Clin Small Anim 49 (2019) 187–209  
<https://doi.org/10.1016/j.cvs.2018.11.001>

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replaced feline urologic syndrome (FUS). Similar to FUS, these terms focus primarily on the lower urinary tract (LUT) system, but do not specifically define the problem.

Clinical signs referable to the LUT of indoor-housed cats have been described in the veterinary literature for nearly a century.<sup>2</sup> The terms FUS and FLUTD were used in the 1970s (FUS<sup>3</sup>) and 1980s (FLUTD<sup>1</sup>) to describe the variable combinations of straining, hematuria, pollakiuria (frequent passage of small amounts of urine), and periuria (urinations outside the litter box) seen in cats. In cats with acute lower urinary tract signs (LUTS), signs recur in 40% to 60% of cats,<sup>4,5</sup> which we define as chronic LUTS (cLUTS).

No definitive urologic explanation for these clinical signs is determined in approximately two-thirds of adult (1–10 years of age) cats with cLUTS; we refer to these patients as having feline idiopathic/interstitial cystitis (FIC). The word “interstitial” was chosen only because of the similarities between cats and humans with interstitial cystitis (now commonly referred to as bladder pain syndrome/interstitial cystitis [BPS/IC]), an idiopathic pelvic pain syndrome of human beings characterized by difficult, painful, and frequent urinations without a diagnosable cause,<sup>6</sup> and often a variety of other health problems.<sup>7</sup> The term “cystitis” is archaic<sup>8</sup>; no significant inflammatory response is seen in the bladder of cats with FIC.<sup>9</sup>

Acronyms, such as FUS or FLUTD, to describe cats with cLUTS provide only a vague description focused on the end organ, rather than a more contemporary understanding of the etiopathogenesis of most cases of cLUTS. One of the authors (C.A.T.B.) has proposed the term “Pandora syndrome” to describe the problems present in some of these cats, for at least two reasons: it does not identify any specific cause or organ; and it seems to capture the dismay and dispute associated with the identification of so many problems outside the organ of interest of any particular subspecialty.<sup>10,11</sup>

Clinical research on cats with cLUTS has identified genetic factors, epigenetic influences, and environmental influences associated with cLUTS<sup>12</sup>; documented that comorbid disorders often occur before the onset of the LUTS<sup>13</sup>; and demonstrated how much systemic involvement can occur in these patients.<sup>14</sup> Whereas invasive (and mostly ineffective) treatments for humans with BPS/IC aim at the bladder, management also is slowly evolving to treat this disorder as a systemic syndrome.<sup>15,16</sup> Similar to humans, evidence has accumulated that additional problems outside the LUT are commonly present in cats with cLUTS.<sup>17</sup> This evidence has led to reconsideration of the causes of the syndrome in these individuals, and to considerable debate about the most appropriate diagnostic and treatment recommendations. Regardless of the name used for this “syndrome,” we urge clinicians to take a global approach when obtaining a history, performing the physical examination, and considering pertinent diagnostics and therapeutics to manage the clinical signs of their patients. However, to avoid confusion, we still refer to this syndrome as FIC, because it was the term used at the time many studies were published.

We currently perceive FIC to be an anxiety disorder, pathology resulting from chronic activation of the central threat response system (CTRS).<sup>10</sup> Persistent activation of this system by the presence of chronic perception of threat that exceeds the cat’s perception of control mobilizes activity in variable combinations of the nervous (sensory, autonomic, and motor), endocrine, and immune systems, which can eventually result in pathology affecting any combination of organ systems.<sup>18</sup>

The variability in response to chronic perception of threat may result from familial differences in organ-specific vulnerability, and to the intensity of exposure to threatening events that can durably sensitize the CTRS to the environment. Such events often occur early in life, even before birth, when the CTRS is most plastic and vulnerable to the events communicated to it through the placenta by its mother.<sup>12</sup> Sufficiently harsh events can sensitize the CTRS at any time of life, however.

## HISTOPATHOLOGY AND BIOMARKERS

Two forms of BPS/IC are recognized in humans, the common (>90% of cases) non-ulcerative (type I) and uncommon (<10%) Hunner ulcer ulcerative form (type II).<sup>19</sup> Most cats with FIC have signs comparable with the type I form, although the type II form has been described in a cat.<sup>20</sup> It is possible that the etiopathogenesis of these two forms is different in cats, as it seems to be in humans. Type II seems to include a conventional inflammatory response, whereas type I might be more associated with neuroendocrine-immune abnormalities (see later). No well-accepted diagnostic test for FIC currently exists, although research evaluating urine and serum biomarkers has been published (none of these biomarkers are currently available).<sup>21–23</sup> Recently, various proinflammatory cytokines and chemokines (eg, CXCL12, interleukin-12, interleukin-18, and FLT3L)<sup>24</sup> were noted to be increased in the serum of cats with FIC. Cystoscopy and biopsies were not obtained in that study to document if any characteristic ulcerative or other inflammatory lesions were present in those cats. Moreover, no evidence permits one to discriminate between these changes being antecedents, consequences, or differences not directly related to the problem. Given other evidence of the success of various therapeutic approaches (discussed later), it seems that these changes may be a consequence of some underlying disorder.

## RESEARCH ON FELINE IDIOPATHIC/INTERSTITIAL CYSTITIS: BLADDER AND BEYOND

Bladder epithelial, called urothelial, cells can respond to various stimuli, including adenosine triphosphate and nitric oxide, which could potentiate inflammation and exacerbate clinical signs in cats with FIC.<sup>25</sup> The bladder (and nonbladder) sensory neurons in cats with FIC exhibit an increased excitability to physical and chemical stimuli as compared with unaffected cats, albeit outside the normal range of bladder pressure.<sup>26</sup>

Sympathoneural-epithelial interactions also seem to play an important role in the permeability of the urothelium. Birder and colleagues<sup>27</sup> have shown that application of norepinephrine to urinary bladder strips induced the release of nitric oxide from the urothelium. Application of capsaicin, the active compound in hot peppers, also resulted in the release of nitric oxide from urothelium, and nervous tissue in the urinary bladder. In light of reports that nitric oxide may increase permeability in the urothelium<sup>28</sup> (and elsewhere),<sup>29,30</sup> these results suggest that some of the sympathetically mediated alterations in permeability may be mediated by norepinephrine via this mechanism.

In humans presenting with cLUTS, urodynamic evaluations are often performed to rule out other LUT diseases, such as overactive bladder (OAB), which could account for the clinical signs. Urodynamic studies in humans have found that patients with BPS/IC had fewer episodes of urge incontinence and shorter duration of symptoms compared with those with OAB.<sup>31</sup> Furthermore they had significantly decreased maximal bladder capacity compared with women with OAB. Although a decrease in bladder compliance has been found in cats with FIC, no evidence of spontaneous bladder contractions (OAB) was noted in female cats with FIC when cystometrograms were evaluated.<sup>32</sup> However, increased urethral closure pressures were noted in cats with FIC compared with healthy cats, despite a lack of clinical signs at the time the studies were performed.

Clinical signs of FIC can wax and wane, and seem to be exacerbated by internal and external stressors.<sup>33</sup> Elevations in catecholamine and decreases in serum cortisol concentrations in cats with FIC compared with healthy cats during times of acute and chronic stress have been reported, suggesting an uncoupling of these two

parameters of the stress response. Based on this research, we believe that FIC may include multiple, complex, and variable abnormalities of the nervous, endocrine, and immune systems that likely affect more than just the bladder.<sup>11,34–36</sup> Enhanced central noradrenergic drive in the face of inadequate adrenocortical restraint seems to be related to maintaining the chronic disease process. These systems seem to be driven by tonically increased hypothalamic corticotropin-releasing factor release, which may represent the outcome of a developmental accident.<sup>37</sup> Treatment strategies that decrease the activity of the CTRS seem to reduce signs of FIC; those that do not address this aspect of the disease seem to be less effective. Until more effective treatments to normalize the responsiveness of this system are available, efforts to reduce input to this system by effective multimodal environmental modification (MEMO) has been shown to effectively reduce clinical signs of FIC and related comorbidities in affected cats (discussed later).<sup>36,38</sup>

It has also become apparent that humans with BPS/IC often overlap or share symptoms commonly associated with other persistent pain disorders, such as irritable bowel syndrome and fibromyalgia, and even OAB.<sup>16</sup> Similarly, cats can present with other comorbidities in addition to the LUTS. A study of healthy cats and cats with FIC found that environmental stressors resulted in increased number of sickness behaviors (eg, vomiting, lethargy, and anorexia) in cats with FIC when the results were controlled for other factors.<sup>36</sup> Furthermore, cats with FIC have a variable combination of comorbid disorders,<sup>17,39,40</sup> such as behavioral, endocrine, cardiovascular, and gastrointestinal problems. Therefore, a complete physical examination and detailed environmental history must be obtained from owners of these cats, rather than restricting focus entirely on the bladder, to appreciate the complexity of some cases.

## RECENT EPIDEMIOLOGIC STUDIES

Lund and colleagues<sup>41</sup> recently reported that obesity ( $P = .004$ ), nervous disposition ( $P = .007$ ), and frequent diet changes ( $P = .025$ ) were found significantly more often in 70 cats with FIC in the final multivariate model of their matched, case-control study when compared with 95 control cats in Norway. Defauw and colleagues,<sup>42</sup> using a retrospective, case-controlled design, found similar results, and also reported that inactive lifestyle and increased threat responsiveness were significantly (all  $P$  values  $< 0.01$ ) more commonly found in 64 cats with FIC than in 64 control cats in Belgium. A more recent case-controlled study of 58 cats with FIC and 281 randomly selected control cats living in a primarily indoor environment in South Korea found that cats with FIC were 2.53 times (odds ratio;  $P = .006$ ) more likely to live in an apartment than in a house, 2.62 times ( $P = .003$ ) more likely to have access only to nonclumping litter, 3.16 times ( $P = .001$ ) more likely to live with other cats, and 4.64 times ( $P < .001$ ) more likely *not* to have a vantage point they could climb on.<sup>43</sup> Although urethral obstruction occurs more commonly in male than in female cats, this is likely caused by differences in the anatomy of the urethra. Underlying FIC is thought to be the cause of urethral obstruction in some, perhaps many, cases.<sup>44</sup> Moreover, the epidemiology of the urethral obstruction in male cats seems broadly similar to that found in most epidemiologic studies of FIC.<sup>45</sup>

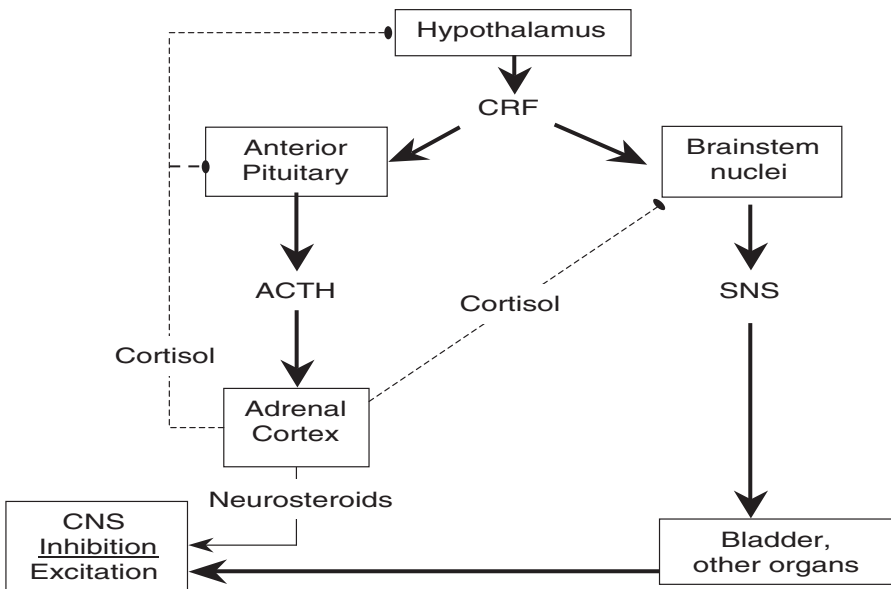
All of these studies provide additional evidence for the presence of complex interactions between susceptible individuals and provocative environments in the development of cLUTS.<sup>33</sup> Knowing these risk factors can help clinicians tailor treatment protocols to the cat's environmental circumstances (see later) or better yet, optimize the environment early in the cat's life to help prevent cLUTS associated with FIC.

Moreover, effective environmental management is an essential part of the responsibility to protect the health and welfare of confined animals (<https://www.avma.org/KB/Resources/Reference/AnimalWelfare/Pages/default.aspx>. Accessed January 8, 2019).<sup>46</sup>

## DIAGNOSTIC EVALUATION OF CATS WITH LOWER URINARY TRACT SIGNS

When choosing the appropriate diagnostic tests for a cat that is presented for evaluation of LUTS, several factors need to be taken into consideration, including the number of episodes the cat has had, the severity of the cat's clinical signs, and the financial limitations of the owner. Because no sensitive, specific, and clinically available test currently exists to diagnose FIC, the diagnosis rests on signalment, history, including inclusion of cat and environmental risk factors as described previously, exclusion of other (common) causes of LUTS, and response to therapy (see [algorithm](#)).

Most adult middle-aged cats with cLUTS are eventually diagnosed with FIC, so we often begin by offering treatment of FIC and monitoring the cat's response, watching carefully for a positive response, particularly if the owner has financial constraints and declines additional diagnostic testing (eg, urinalysis, imaging). If the cat does not improve, or if clinical signs return within days to weeks despite implementation of appropriate MEMO, we recommend abdominal radiography because the next most common differential in cats with cLUTS is urinary stone disease. Abdominal radiography, including the entire urinary system from the proximal pole of the kidney to beyond the end of the distal urethra, helps detect radiodense stones; approximately 20% of cats with LUTS have bladder stones. A urinalysis and urine bacterial culture should be evaluated at least once in cats with cLUTS if possible, but most young, otherwise healthy cats do not have a true bacterial cystitis. Furthermore, there is no sound evidence to support culture of the urine after urinary catheter removal from cats with obstructive FIC unless clinical signs have returned or progressed.



Antimicrobial therapy is not recommended unless the cat has LUTS in association with a positive urine culture collected by cystocentesis. Advanced diagnostic tests, such as contrast cystourethrography, abdominal ultrasonography, and even cystoscopy, are performed in recurrent cases to be certain no other disease that could account for the clinical signs is present. The latter is rarely required or performed in cats suspected of having FIC.

## TREATMENT OF CATS WITH CHRONIC LOWER URINARY TRACT SIGNS

### *Acute Treatment*

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LUTS resolve in 85% of cats within 2 to 7 days, with or without treatment. Most aspects of acute therapy have not been adequately tested to permit evidence-based recommendations. Because of the presumed threat sensitivity of cats with FIC, we try to use pertinent trauma-informed care principles with clients and their cats (eg, safety, predictability, empowerment, choice, shared decision making).<sup>47</sup> Low-stress handling techniques and predictable nursing care can reduce cats' perception of threat.<sup>35,48</sup> If the patient is hospitalized, careful consideration of the quality of the cage environment may help the cat cope with this confinement.<sup>48,49</sup> Cats tend to form attachments to places, so confinement in places where they do not feel safe can adversely affect their behavior and physiology. Enriched conditions permit cats to cope with their surroundings and feel more safe in their space.

Factors inside and outside their cage can affect the welfare of cats housed in veterinary hospitals.<sup>35</sup> Inside the cage, each cat needs these resources at its disposal:

- A place to hide: Cats like places to hide to escape threats, keep warm, and to scratch and perch on. We place these at the back of the cage to try to help the cat feel safer.
- Bedding: Cover the bottom of the cage completely. Bare surfaces can be cold and uncomfortable. Bedding with the cat's and owner's scent also may reduce cats' perception of threat. Change bedding only when soiled (rather than daily); most cats seem to prefer familiar bedding.
- Food and water: Provide the cat's usual food if feasible, and put food and water at the back of the cage as close as possible to its hiding place to help the cat feel safer.
- Litter box: Place at the front of the cage, because cats use it less frequently than (and only after) they use eating and drinking bowls.
- Other things: Provide music (played softly), and extra attention like brushing or playing from a familiar, dedicated person whenever possible.
- Door: Cover as much of the door of the cage as possible to reduce potentially threatening stimulation.

Factors outside the cage also are stressful for confined cats.<sup>48</sup> These can include the following:<sup>50</sup>

- Lights: Put on a timer for predictable lighting from day to day if natural light is not available, or turn lights on and off manually at the same time each day. Do NOT turn lights on and off each time someone goes in and out of the ward/room.
- Noise: Keep levels in the ward to a minimum (<60 dB, a quiet conversational level, can be measured with smartphone apps).
- Odors: Minimize smells from dogs, other cats, perfumes, alcohol (from hand rubs), cigarettes, cleaning chemicals (including laundry detergent); all these are aversive and stressful, especially to cats confined in a cage where they cannot move away from the odors.

- Temperature: Cats prefer warm, 85°F to 100°F, temperatures.<sup>51</sup> Provide bedding that allows cats cocoon to retain warmth if they choose to do so.
- Daily routine: To the extent possible, perform cleaning, feeding, and treatment procedures at the same time each day, preferably by the same person to increase predictability of the environment for the cat. Return cage furnishings to the same place after spot-cleaning, and house cats in the same cage throughout their stay.
- Low stress handling: Use these techniques to minimize activation of the cat's CTRS.

Behaviors signaling that something may be wrong with caged cats include resting in litter boxes, and cages that show no use since the last cleaning or are in disarray. Sickness behaviors also are cause for concern.<sup>36</sup> These include variable combinations of vomiting, diarrhea or soft feces, no eliminations in 24 hours, urinating or defecating out of the litter box, anorexia or decreased appetite, lethargy, and not grooming.<sup>36</sup>

One can recognize when a cat feels threatened by observing changes in its physiology and behavior, recognizing that the changes in any one cat might be different from those of another that feels similarly threatened. Any effectiveness of any housing situation or handling technique is evaluated by assessing physiologic and behavioral parameters in the cat before and after it is applied. Physiologic and behavioral parameters associated with perception of threat include variable combinations of the following; their converse suggest perception of safety:

Physiologic parameters	
Increase in	Presence of
<ul style="list-style-type: none"> <li>• Pupil diameter</li> <li>• Respiratory rate</li> <li>• Temperature</li> <li>• Heart rate</li> <li>• Blood pressure</li> </ul>	<ul style="list-style-type: none"> <li>• "Sweaty" paws</li> <li>• Excessive shedding</li> <li>• Flushing of the skin</li> <li>• Anxious lip-licking</li> </ul>

Behavioral parameters/body postures	
Increases in withdrawal behaviors	Decreases in affiliative ("approach") behaviors
<ul style="list-style-type: none"> <li>• Immobility: hiding, cowering, or freezing behaviors</li> <li>• Attempts to run away or avoid handlers</li> <li>• Defensive aggression (hissing, growling, spitting, tail twitching, ear flicking, scratching, biting)</li> </ul>	<ul style="list-style-type: none"> <li>• Friendly approach to caregivers</li> <li>• Purring, kneading, rubbing</li> <li>• Interest in food</li> <li>• Relaxed body postures, normal eliminations</li> <li>• Increased effectiveness of the technique with repeated use</li> </ul>

### **Acute Pharmacotherapy**

Analgesic therapy for acute pain management is provided when clinically indicated, which seems prudent given the clinical manifestations in cats and the pain described in humans with the syndrome. Use of nonsteroidal anti-inflammatory drugs has been suggested, but with disappointing results, at least in obstructive FIC.<sup>52</sup> Because of the risk for dehydration-associated reductions in blood flow to the kidneys and the potential for acute kidney injury, these medications might increase the risk for adverse

outcomes. Moreover, nonsteroidal anti-inflammatory drugs have been found to be ineffective for pain management of patients with BPS/IC, and are not part of contemporary therapeutic guidelines for patients with this syndrome.<sup>6,53</sup> Other analgesics also have been used, but not yet been subjected to properly controlled clinical trials to our knowledge.

## **CHRONIC TREATMENT**

### ***Treating the Client***

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A diagnosis of FIC means that one has identified an anxiety and excluded (to the extent possible) other causes for the signs. In our experience, the most important consideration for a successful outcome for cats with FIC is effective and empathic client communication.<sup>54</sup> After performing a complete evaluation of the cat and concluding that FIC is likely to be present (pending observation of responsiveness to MEMO), we can explain to the client that although no cure currently is available, appropriate MEMO and other therapeutic interventions can generally keep the cat's clinical signs to a minimum and increase the disease-free interval, and that most care can be provided in collaboration with a trained technician. We also demonstrate empathy by listening carefully to the client's (often frustrated) story of the effects of having a cat with FIC, provide a satisfactory explanation for the sources of the signs, express care and concern for the situation, and enhance the client's perception of control. Effective doctor-patient interactions seem to enhance patient adherence to treatments, and quality of life outcomes of therapy.<sup>55</sup> We can then prescribe any therapies appropriate to the presenting manifestations, and when possible introduce the client to the technician or other staff member trained to care for cats with FIC, who coach the client to implement MEMO for the patient. The formality of this introduction demonstrates that we intend to sustain the partnership with the client through our technical support staff to gain control of the patient's clinical signs.

### ***Treating the Environment: Multimodal Environmental Modification***

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Environmental conditions are known to affect the behavior and health of animals,<sup>56,57</sup> particularly captive animals.<sup>50,58,59</sup> Just as water is primary therapy for prevention of urinary stone recurrence,<sup>60</sup> MEMO is primary therapy for prevention of recurrence of signs of FIC. Effective MEMO has been shown to provide relief in a variety of animal models of chronic pain.<sup>18,57,61</sup> If cats with FIC have a sensitized CTRS, then treatments that increase their perception of control and reduce their perception of threat are more likely to be effective than those that do not. Effective MEMO creates conditions that permit the patient to feel safe, and to have unrestricted access to species-appropriate novelty, activity, and interactions with other animals (including humans). Effective MEMO for cats means provision of all necessary resources, refinement of interactions with owners, a tolerable intensity of conflict, and thoughtful institution of changes to the cat's environment (its territory). It also extends the "one + one" rule traditionally applied to litter boxes (one for each cat in the home, plus one more) to all pertinent resources (particularly resting areas, and food, water, and litter containers) in the home.

This opinion is based on the documented neuroendocrine abnormalities suffered by cats with FIC,<sup>23,34,62</sup> and on our research and clinical experience. Although we are not aware that a particular resource list has been validated for indoor-housed cats, some recommendations are available. We have assembled a provisional list in **Box 1** that might be used to guide consideration of these parameters for each of their cats. The following tentative recommendations are organized to follow the table; other



**Box 1****A checklist of confined cats' needs**

- Safe places to rest and sleep, preferably including a carrier as one option.
- An environment that accommodates all sensory modalities, including gustatory, visual, auditory, tactile, and olfactory.
- Satisfactory foods, which accommodate the preferences of the owner and the cat.
- Daily opportunities for the cat to play and engage in predatory behavior.
- Multiple and separated areas in multicat households for key environmental resources (resting and sleeping, food, water, toileting, scratching, climbing, and play).
- Changes in environmental resources offered as choices to allow the cat to express its preferences.
- As positive, consistent, and predictable an environment as possible.
- Positive, consistent, and predictable daily human-cat social interaction.

environmental questionnaires and suggestions are available in the many excellent publications about cat housing and behavior that currently are available.<sup>63,64</sup>

A prospective observational study that evaluated client-reported recurrence rates of LUTS (and other behavioral problems) in cats with FIC after MEMO therapy suggested that this form of therapy is beneficial for cats with FIC. Clients were asked to complete a detailed environmental history sheet (a similar one is found in **Fig. 1**), and specific recommendations for MEMO based on this assessment were made for each client.<sup>38</sup> Cases were followed for 10 months, primarily by telephone contact. Significant ( $P < .05$ ) reductions in LUTS, fearfulness, nervousness, signs referable to the respiratory tract, and a trend ( $P < .1$ ) toward reduced aggressive behavior and signs referable to the lower intestinal tract were identified. Additionally, experimental studies of rodents subjected to early adverse experience have documented psychoneuroendocrine abnormalities, which may be compensated for, if not repaired by, MEMO.<sup>65–67</sup> Not all cats require intense MEMO therapy, so clinicians can tailor the MEMO changes implemented based on the cats' needs and owner's desire and commitment to this process. Because of the lack of controlled trials, it currently is not possible to prioritize the importance of any of these suggestions provided, or to predict which would be most appropriate in any particular situation. Appropriately designed epidemiologic studies might be able to identify particularly important factors (discussed previously), after which intervention trials could be conducted to determine their effectiveness in circumstances where owners successfully implemented the suggested changes.

**Space**

Provide safe resting places for each cat. Using an inviting soft fabric or hard plastic cat carrier for one of these places also helps habituate the cat to its carrier and can facilitate transport when necessary. Some cats also enjoy using beds heated with warming pads made specifically for pet beds. Cats interact with the physical structures and other animals, including humans, in their environment. The physical environment should include opportunities for scratching (horizontal and vertical may be necessary), climbing, and hiding in addition to resting. Cats seem to prefer to monitor their surroundings from elevated vantage points, so climbing frames, hammocks, platforms, raised walkways, shelves, or window seats may appeal to them. Playing a sound source to habituate cats to sudden changes in sound and human voices in their

### Health History Questionnaire – (one for each cat)

Your Last Name: \_\_\_\_\_ This cat's name: \_\_\_\_\_






Your ZIP code: \_\_\_\_\_ Today's Date: \_\_\_\_\_

Description: Breed: \_\_\_\_\_ Color: \_\_\_\_\_ Birthdate \_\_\_\_\_ Weight: \_\_\_\_\_  lb.  kg

Owned for: \_\_\_\_\_ years;  Male  Female Neutered?  No  Yes if yes, Date: \_\_\_\_\_

Declawed?  N  Y If yes, Front paws only  All four paws

Body Condition (please check box that looks most like this cat):

<input type="checkbox"/> Skinny	<input type="checkbox"/> Lean	<input type="checkbox"/> Moderate	<input type="checkbox"/> Stout	<input type="checkbox"/> Obese
				

Diet: please include the name of the food, the company that makes it, and the flavor of the food

Food: \_\_\_\_\_ % of TOTAL daily food eaten by this cat

Wet: \_\_\_\_\_  None  25%  50%  75%  100%

Dry: \_\_\_\_\_  None  25%  50%  75%  100%

Other: \_\_\_\_\_  None  25%  50%  75%  100%

Where did you get this cat?

Offspring from a pet I already own(ed)  From a shelter/rescue organization

From a friend  Stray/orphan

From a breeder  Gift

From a pet shop  Other (please describe)

How many hours a day, on average, does this cat spend indoors?	<input type="checkbox"/> 24 - indoor Only	<input type="checkbox"/> 18-24	<input type="checkbox"/> 12-18	<input type="checkbox"/> 6-12	<input type="checkbox"/> 0-6
Is time outside supervised?	<input type="checkbox"/> Not applicable		<input type="checkbox"/> Yes	<input type="checkbox"/> No	

We live in:  Apartment or condominium building  Standalone home

Other (please describe) \_\_\_\_\_

Total Number of Cats \_\_\_\_\_ Dogs \_\_\_\_\_ Other Pets \_\_\_\_\_ People \_\_\_\_\_ in your home

If you have more than one cat, are they related?  No

Yes:  Littermate  Sibling  Parent-Offspring  Other \_\_\_\_\_

How many hours each day are you in sight of this cat? \_\_\_\_\_ hours/day.

How many minutes each day do you pet/hold/sit near to this cat? \_\_\_\_\_ minutes/day.

How many minutes each day do you spend playing with this cat? \_\_\_\_\_ minutes/day.

Fig. 1. Environmental survey for indoor-housed cats.<sup>1</sup> Female pronouns are used in honor of Bastet, the Egyptian cat goddess revered for her hunting prowess and motherly nurturing skills. We love male cats too, and everything also applies to them.

surroundings also has been recommended, and videos to provide visual stimulation are available.

#### Food

As a part of the MEMO therapy, dietary modifications may be warranted and should be discussed with clients. Efforts to acidify the urine using dry foods have no proven value in the treatment of cats with FIC; however, if pronounced struvite crystalluria is present in an obstructed male cat (ie, obstructive FIC), a diet formulated to produce a urinary pH less than the relative supersaturation for struvite may be indicated. A diet high in moisture (eg, canned food) also may help prevent recurrences, but studies to evaluate

### What Does Your Cat Do

	Thinking about the last 4 weeks My cat:	Almost always	Repeatedly	Often	Some times	Seldom	Rarely	Never
1	Moves around our home free to explore, climb, stretch, or play as she <sup>1</sup> chooses.							
2	Approaches people to be sociable.							
3	Avoids being held, picked up, handled or petted.							
4	Actively plays with toys, others, or self.							
5	Uses a climbing tree/elevated vantage point to rest or have an overview of her surroundings.							
6	Is easily startled.							
7	Uses an "approved" object to scratch on.							
8	Remains calm when left alone.							
9	Eats and drinks small amounts calmly often throughout the 24-hour day.							
10	Tries to escape to the outdoors.							
11	Cries or paces at doors to the outside.							
12	Chase or attacks people's hands, feet, or ankles.							
13	Chase or attacks other animals.							
14	Lies on side while relaxing.							
15	Growls, hisses, bites or scratches when approached.							
16	Makes positive sounds, like purring, chirping or friendly meowing.							
		Almost always	Repeatedly	Often	Some times	Seldom	Rarely	Never
17	I correct/punish this cat for behaviors that annoy me							
18	Our home is quiet.							
19	Our household schedule is predictable from day to day.							

<sup>1</sup> I use female pronouns in honor of Bastet, the Egyptian cat goddess revered both for her hunting prowess and motherly nurturing skills. We love male cats too, and everything also applies to them.

Fig. 1. (continued).

this effect have not been conclusive to date. Although we have demonstrated that feeding wet food is not essential in enriched environments,<sup>36,38</sup> it may be more beneficial in environments that are less enriched, although to our knowledge this has not been studied in a controlled trial. Cats may find wet food to be preferable because of the increased water content, or to a more natural "mouth feel," whereas some cats seem to strongly to prefer dry foods. Obesity often is associated with FIC, so implementing a MEMO-based weight loss program also may be of benefit, if clinically indicated, but should be approached cautiously to avoid overwhelming the client with recommendations.<sup>68</sup>

### Your Cat's Environment – (one for each household, or each cat if different)

We ask the following questions to get a better idea of your home from your cat's point of view. In homes with more than one cat, some cats like to have their "stuff" (resting area, food and water, litter box, etc.) **out of sight of all other cat's stuff**, so think about where each cat's stuff is if you have more than one cat as you fill out the form.

#	Space	Yes	No
1	Each cat has a personal space that provides her with safety and security.		
2	Each personal space is located such that another animal or person cannot sneak up on your cat(s) while they are resting.		
3	Each personal space is located away from appliances or air ducts that could come on unexpectedly while your cat(s) are resting.		
4	Scented candles, incense, perfume or other fragrances are commonly used in our home.		
5	There are sights (like other animals), sounds (like construction or traffic) or smells (like other animals) outside our home that might disturb our cat(s).		
#	Food and Water	Yes	No
6	Each cat has her own food bowl.		
7	Each cat has her own water bowl.		
8	Both food and water bowls are located out of sight of all other cat's bowls.		
9	Both food and water bowls are located at least 3 feet (1 meter) from the nearest litter box.		
10	All bowls are located such that another animal or person cannot sneak up on each cat while she eats or drinks.		
11	All bowls are located away from appliances or air ducts that could come on unexpectedly while any cat is eating.		
12	Do you provide any food in food puzzles?		
#	Litter boxes	Yes	No
13	There is at least 1 box per cat + 1 extra in our home.		
14	Each cat's box is located in a convenient, well-ventilated place that still gives her some privacy while using it.		
15	Boxes are located so another animal or human cannot sneak up on each cat during use.		
16	Boxes are located away from appliances or air ducts that could come on unexpectedly during use.		
17	Boxes are as long as each cat's body, from the tip of the nose to the tip of the tail.		
18	Some boxes are covered.		
19	Unscented, clumping litter is used.		
20	There is at least enough litter in each box so each cat can scratch around without hitting bottom.		
21	Each litter box is scooped as soon after use as possible, or at least daily.		

Please write additional comments on or questions about any of the items in this form below, including the question #. \_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

Fig. 1. (continued).

Diets containing additives that purportedly decrease anxiety (eg,  $\alpha$ -casozepine and L-tryptophan) in stressed cats and those tailored for FIC management also are marketed for cats, but the evidence for their effectiveness in management of FIC have not been well investigated, and their general salutary effects, if any, seem modest.<sup>69,70</sup> Moreover, studies have shown that many cats with FIC are effectively managed without any diet change.<sup>36,38,71</sup> In most cases we recommend that clients choose whichever (Association of American Feed Control Officials labeled) diets fit their personal preferences, and then offer a few examples of these at mealtime so their cat can express its preferences. We recommend this to minimize the effects of client's and patient's perception of diet on the activation of their CTRS.

If a diet change is appropriate, offering the new diet in a separate, adjacent container rather than removing the usual food and replacing it with the new food

### Your Cat's Health

**Directions:** Please use the following choices to describe how often this cat has done each item, both in the past years, **and** in the last 4 weeks.

In the PAST, how often has this cat:		Score	In the LAST 4 WEEKS, how often has this cat:	
Score: 0=never, 1=at least once, 2=at least yearly, 3=a few times a year, 4=at least monthly				
Wheezed				
Sneezed				
Had discharge from nose				
Had discharge from eyes				
Had difficulty breathing				
Eaten more or less than usual				
Vomited <input type="checkbox"/> food <input type="checkbox"/> hair <input type="checkbox"/> bile <input type="checkbox"/> other				
Had diarrhea				
Had constipation				
Defecated outside the litter box				
Urinated outside the litter box				
Sprayed urine				
Groomed more than cats usually do				
Shed more than cats usually do				
Howled more than cats usually do				
Scratched herself more than cats usually do				

Please check any of the following diseases your veterinarian has diagnosed in this cat, and the date of diagnosis:

Disease	Date	Disease	Date
<input type="checkbox"/> Periodontal (dental) disease		<input type="checkbox"/> Asthma	
<input type="checkbox"/> Inflammatory bowel disease		<input type="checkbox"/> Chronic skin disease	
<input type="checkbox"/> Allergies		<input type="checkbox"/> Diabetes mellitus	
<input type="checkbox"/> Cardiomyopathy (heart problems)		<input type="checkbox"/> Obesity	
<input type="checkbox"/> Chronic dental disease		<input type="checkbox"/> Respiratory tract infections	
<input type="checkbox"/> Chronic kidney disease		<input type="checkbox"/> Urinary stone disease	
<input type="checkbox"/> Other _____			

Please provide any additional comments about this cat's health below:

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Fig. 1. (continued).

permits the cat to express its preference. All the cat's needs must be taken into consideration when making dietary and environmental recommendations.

Behavioral and ethological research suggest that cats prefer to eat individually in a quiet location where they are not startled by other animals, sudden movement, or activity of an air duct or appliance that may begin operation unexpectedly.<sup>72,73</sup> Natural feline feeding behavior also includes predatory activities, such as stalking and pouncing. These may be simulated by hiding small amounts of food around the house, or by putting dry food in a food puzzle from which the cat has to extract individual pieces or move to release the food pieces (if such interventions appeal to the cat).<sup>74</sup> When a diet change seems appropriate, we only attempt to implement it after the

cat has returned home and is feeling better to reduce the risk of inducing a learned aversion to the new food.

### **Water**

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Some cats also seem to have preferences for water that can be investigated. Water-related factors to consider include freshness, taste, movement (water fountains, dripping faucets, or aquarium pump-bubbled air into a bowl), and shape of container (some cats seem to resent having their vibrissae touch the sides of the container when drinking). As with foods, changes in water-related factors should be offered in such a way that permits the cat to express its preferences. Additionally, food and water bowls should be cleaned regularly unless individual preference suggests otherwise.

### **Play**

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Some cats seem to prefer to be petted and groomed, whereas others may prefer play interactions with owners.<sup>75</sup> Cats also are easily trained to perform behaviors (tricks); owners just need to understand that cats respond much better to praise than to force, and seem to be more amenable to learning if the behavior is shaped before feeding. Cats also may enjoy playing with toys, particularly those that are small, move, and that mimic prey characteristics. Many cats also prefer novelty, so a variety of toys should be provided, and rotated or replaced regularly to sustain their interest.

Some cats also seem to have specific prey preferences. For example, some cats prefer to chase birds, whereas others may prefer to chase mice or bugs. Identifying a cat's prey preference allows one to buy or make toys that the cat is more likely to play with. Prey preference are identified by paying close attention to the cat's reaction to toys with specific qualities, such as those that resemble birds (feather toys), small mammals (furry mice), or insects (laser pointers, pieces of dry food) presented one at a time or together.

### **Litter Boxes**

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Litter boxes should be provided in different locations throughout the house to the extent possible, particularly in multiple cat households.<sup>76</sup> Placing litter boxes in quiet, convenient locations that provide an escape route if necessary for the cat could help improve conditions for normal elimination behaviors. If different litters are offered, it may be preferable to test the cat's preferences by providing them in separate boxes, because individual preferences for litter type have been documented. For cats with a history of urinary problems, unscented clumping litter may be preferred.<sup>77</sup> Litter boxes should be cleaned regularly and replaced; some cats seem sensitive to dirty litter boxes. Litter box size and whether or not it is open or covered also may be important to some cats.<sup>78,79</sup>

### **Conflict**

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Conflict can develop between cats, and between cats and other animals and people in the home.<sup>80</sup> When cats become threatened, they seem to respond in an attempt to restore their perception of control. During such responses, some cats become aggressive, some become withdrawn, and some become ill. In our experience, conflict is the most common reason that some health problems occur in households with multiple cats confined indoors. With a little practice, one can recognize the signs of conflict and estimate its potential role in exacerbation of signs of FIC. Owners usually can identify the causes after the signs of conflict are explained to them. Once this has been done, clients often are well on their way to reducing the intensity of conflict.

Of course, some conflict between housemates is normal, regardless of species. The goal is to reduce unhealthy conflict to a more manageable level for the cats involved.

Signs of conflict (**Table 1**) between cats are open or silent. Signs of open conflict are easy to recognize; the cats may stalk each other, hiss, and turn sideways with legs straight and hair standing on end up to make themselves look larger. If neither cat backs down, the displays may increase to swatting, wrestling, and biting. The signs of silent conflict are so subtle they are easily missed or ignored by owners. The cat creating the conflict (assertive cat) is identified as the one that never backs away from other (threatened) cats, denies other cats' access to resources, stares at other cats, and lowers its head and neck while elevating its hindquarters as it approaches less confident cats. The hair along its back, on its tail, and tail base may stand on end, although not to the extent of cats engaged in open conflict, and it may emit a low growl. The assertive cat eventually may only have to approach or stare at a threatened cat for it to leave a resource, such as food or a litter box. If the threatened cat tries to use the resource later, the assertive cat's presence alone may be enough to make it flee. Because cats do not seem to possess distinct dominance hierarchies or conflict resolution strategies, threatened cats may attempt to circumvent agonistic encounters by avoiding other cats, by decreasing their activity, or both. Threatened cats often spend increasingly large amounts of time away from the family, staying in areas of the house that others do not use, or they attempt to interact with family members only when the assertive cat is elsewhere.

The signs of conflict can result from two types of conflict: offensive and defensive. In offensive conflict, the assertive cat moves closer to the other cats, and to control the interaction. In defensive conflict situations, a threatened cat attempts to increase the distance between itself and whatever it perceives to be a threat. Although cats engaged in either type of conflict may spray or eliminate outside the litter box, we find that threatened cats are more likely to develop FIC.

The most common cause of conflict between indoor-housed cats that we identify is competition for resources. Cats may engage in open or silent conflict over space, food, water, litter boxes, perches, sunny areas, safe places where the cat can watch its environment, or attention from people. There may be no obvious limitation to access to

<b>Table 1</b> <b>Signs of silent conflict between cats</b>	
<i>The Assertive Cat</i>	<i>The Threatened Cat</i>
Never backs away from other cats	Spends large amounts of time hiding or away from the family
Stares at other cats	Avoids eye contact with other cats
Denies other cats access resources	Yields resources to other cats
Rub cheeks, head, chin, and tail on people, doorways, and furniture at cat height	
<i>When it sees the threatened cat</i>	<i>When it sees the assertive cat</i>
Lowers its head and neck while elevating its hindquarters and stalks the other cat	Crouches, may cower, may then flee
Piloerects the hair along its back, tail base, and tail	
Growls	Does not vocalize
May spray	May spray
	May develop cystitis or other disease problem

these resources for conflict to develop. The change may only be the cat's perceptions of how much control it wants over the environment or its housemates' behaviors.

Open conflict is most likely to occur when a new cat is introduced into the house, and when cats that have known each other since kittenhood reach social maturity. Conflict occurring when a new cat is introduced is easy to understand, and good directions are available from many sources for introducing the new cat to the current residents.<sup>81</sup> Clients may be puzzled by conflict that starts when one of their cats becomes socially mature, or when a socially mature cat perceives that one of its housemates is becoming socially mature. Cats become socially mature between 2 and 5 years of age, and may start to take some control of the social groups and their activities. These actions can lead to open conflict between males, between females, or between males and females. Although clients may be surprised, "because they lived so well together for the first few years of their lives," cat's perceptions of resource needs may expand with social maturity.

Cats that are familiar with each other but unevenly matched often show conflict in more subtle ways. One of the cats in the conflict asserts itself, and another cat is threatened by this cat's actions. Silent conflicts may not even be recognized until the threatened cat begins to hide from the assertive cat, to hiss or fight back when it sees the other cat, or when it develops a health problem.

In addition to the signs of conflict described previously, the assertive cat is identified by its marking behavior. These cats rub their cheeks, head, chin, and tail on people, doorways, and furniture at cat height. Unfortunately, silent conflict can also involve urine; including marking by the assertive or the threatened cat, and FIC in the threatened cat. Conflict-related urine marking can include spraying, when the cat treads and kneads, raises its tail, and flicks the tip of it while spraying urine on a vertical surface or squatting and urinating outside the litter box (nonspray marking). Both males and females may spray, and although neutering reduces the frequency of spraying, it cannot eliminate the behavior. Conflict-related urine marking is exhibited by either the assertive or threatened cat, but in our experience, FIC usually occurs in the threatened cat; we have even seen threatened male cats spray bloody urine. Cats that urinate on bedspreads or other elevated, open places may do so because their access to the litter box is restricted by another cat, or if they are afraid to use the box because it is placed such that a quick escape from another cat might not be possible.<sup>64</sup>

Treatment of conflict between cats involves providing a separate set of resources for each cat, preferably in locations where the cats can use them without being seen by other cats. This lets the cats avoid each other if they choose to without being deprived of an essential resource. Conflict also is reduced by neutering all of the cats, and by keeping all nails trimmed as short as practicable. Whenever the cats involved in the conflict cannot be directly supervised, they may need to be separated. This may mean that some of the cats in the household can stay together, but that the threatened cat is provided a refuge from the other cats. This room should contain all necessary resources for the cat staying in it. In severe cases, one or more of the cats may need to be rehomed to avoid euthanasia.

Cats in nature use more space than the average house or apartment affords them. The addition of elevated spaces, such as shelves, "kitty condos," cardboard boxes, beds, or crates may provide enough space to reduce conflict to a tolerable level. In severe situations, some cats may benefit from behavior-modifying medications. In our experience, however, medication can help only after environmental enrichment has occurred, it cannot replace it.

The cats involved in the conflict may never be "best friends," but they usually can live together without showing signs of conflict or conflict-related disease. In severe



cases, a behaviorist may be consulted for assistance in desensitizing and counterconditioning of cats in conflict so they can share the same spaces more comfortably if this is desired.

Conflict with other animals, dogs, children, or adults is straightforward. In addition to being solitary hunters of small prey, cats are small prey themselves for other carnivores, including dogs. Regardless of how sure the client is that others in the home will not hurt the cat, to the cat they may represent a threat. Providing the cat ways to escape at any time, including to vertical safe spaces out of reach of other pets and small children, often reduces its perception of threat to tolerable levels. For older children and adults, it usually suffices to explain that cats may not understand rough treatment as play, but as a predatory threat.

### ***Chronic Pharmacotherapy***

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A variety of drugs have been recommended for use in cats with FIC, but to our knowledge no studies comparing their effectiveness with that of MEMO have been published. There also are hazards associated with drug therapy of cats, which include the aversion of many cats to chronic administration of oral medications, and potential unwanted side effects. With regard to drugs targeting anxiety in general, a recent review of behavioral psychopharmacology in cats<sup>82</sup> reminds us that, "There are no approved behavioral drugs for cats. Using any of the previously mentioned medications for purposes other than the indications listed on the label and the use of any psychoactive medication not listed previously is considered extra label use and falls under the rules of the Animal Medicinal Drug Use Clarification Act of 1994 and its implementing regulations." In fact, many drugs used for FIC are considered "off-label," and owner consent should be obtained before therapy. The review goes on to speculate that maropitant (Cerenia-Zoetis) "has the potential for many additional uses including as an adjunct medication for the treatment of pain and as a mediator of the stress response during handling and hospitalization." Unfortunately, there is no published evidence to support this speculation for cats, and currently available studies in other species suggest that effectiveness in the situations described is not highly likely.<sup>83</sup> There also is one (manufacturer-funded) 4-week study<sup>84</sup> of alpha S1 casein (Zylkene) in anxious cats, but the statistics reported leave one skeptical of the results, and no studies of cats with FIC have been conducted to our knowledge.

Although psychoactive drugs should not be used for cats on initial presentation for acute care of FIC,<sup>85</sup> they may be considered for cats if addressing their environmental needs does not resolve their clinical signs. We consider the use of tricyclic antidepressant and related drugs to be alternatives to euthanasia; to be used only when other approaches have failed. For example, amitriptyline (2.5–7.5 mg/cat PO every 24 hours) was evaluated in an open, non-placebo-controlled trial. It seemed to reduce clinical signs in some cats with severe, refractory FIC.<sup>86</sup> This drug, or clomipramine, another tricyclic antidepressant (0.25–0.5 mg/kg PO every 24 hours), may need to be administered for weeks before a beneficial effect may be noted. If no improvements are noted, or medicating the cat is too stressful (for the owner or the cat), these drugs should be withdrawn gradually, over a period of 1 to 2 weeks. Side effects of the tricyclic antidepressants include sedation, lethargy, weight gain, and urine retention. Because of the possibility of urine retention, we advise monitoring the cat for stone development if clinical signs recur after receiving this class of drugs for an extended period. Fluoxetine (0.5–1 mg/kg PO every 24 hours) is a selective serotonin reuptake inhibitor. It has been shown to decrease signs of urine marking in cats.<sup>87</sup> This drug should also not be abruptly stopped. Selective serotonin reuptake inhibitor side effects can include behavior changes, such as anxiety, and sleep disturbances.

Pentosan polysulfate sodium is a semisynthetic carbohydrate derivative similar to glycosaminoglycans that is also approved for humans with BPS/IC. A multicentered, placebo-controlled, masked study in cats found no significant differences when comparing pentosan polysulfate sodium with placebo.<sup>88</sup> However, all groups had clinical benefit, suggesting a strong placebo effect. All medication was provided to the cat in a food treat, leading some of the authors of the study to speculate that improving the interaction and environmental needs of the cat may inadvertently have contributed to the positive outcomes noted in all groups. Similar findings were reported in two other studies evaluating glycosaminoglycan therapy in cats with FIC,<sup>89,90</sup> and pentosan polysulfate has been shown to be equivalent to placebo in humans with BPS/IC.<sup>91,92</sup>

## ADDITIONAL APPROACHES

### *Pheromones and Other Scents*

Five facial pheromone fractions have been isolated from cats; cats deposit the “F3” fraction on prominent objects (including humans) by rubbing against the object when the cat feels safe and at ease.<sup>93–95</sup> Feliway, a synthetic analogue of this occurring feline facial pheromone, was developed to decrease anxiety-related behaviors of cats. Treatment with this pheromone (most often in company-funded studies) has been reported to reduce the amount of anxiety experienced by cats in unfamiliar circumstances, a response that may be helpful to these patients and their owners. Decreased spraying in multicat households, decreased marking, and a significant decrease in scratching behavior also has been reported subsequent to its use. In a pilot study evaluating Feliway in cats with FIC, no significant decrease in the number of days that clinical signs were exhibited was found.<sup>96</sup> Moreover, recent systematic reviews<sup>97,98</sup> and studies<sup>99</sup> have questioned its efficacy.

Another recent study reported that some cats may enjoy other scents, including catnip, silver vine, Tatarian honeysuckle, and valerian (a constituent of Feliway spray, but not diffusers). Another recent study reported that pet cat’s preferences were: owner social interaction with the owner (50%) = food (37%) > toys (11%) > scent (2%). Preference for food was not different from toys, but greater than for scent.<sup>100</sup> Although social interaction with humans was the most-preferred stimulus category for most cats, followed by food, there was clear individual variability among the cats in preference, demonstrating once again the importance of “asking the cat” by offering changes as choices.

## SUMMARY

Many indoor-housed cats seem to survive perfectly well by accommodating to less than perfect surroundings. The neuroendocrine-immune abnormalities in the cats with FIC, however, do not seem to permit the adaptive capacity of healthy cats, so these cats may be considered a separate population with greater sensitivity to their environments. Early intervention with MEMO could help prevent an initial episode, or to prevent a single episode from progressing to a chronic disease. Furthermore, gaining a better understanding of FIC (including the most accurate descriptive terminology) may help researchers, veterinarians, pet food companies, and clients develop and tailor the best possible approaches to management of these cat’s unique health and welfare needs.

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