Feline lower urinary tract disease (FLUTD) describes a collection of conditions that can affect the bladder and urethra of cats. Feline idiopathic cystitis (FIC) is the most common form of FLUTD; approximately ⅔ of cats with FLUTD have FIC.

OVERVIEW
Prevalence & Risk Factors
- FLUTD is responsible for 7% to 8% of all feline admissions to veterinary hospitals, and has been reported in 0.49% to 1.26% of all cats.¹²
- FLUTD appears to be equally prevalent in male and female cats.
- Both overweight cats and indoor cats are considered to be at greater risk for development of FLUTD; however, urinary habits of outdoor cats may not be observed as thoroughly.
- Most FLUTD first occurs in cats between 2 and 6 years of age.³
- Approximately 50% of cats that experience 1 episode of FLUTD will have a recurrence.⁴

Common Causes
FLUTD can be divided into 2 broad categories—based on presence or absence of an identifiable cause. Common causes of FLUTD, or conditions with clinical signs that mimic the disease, include:
- Anatomic abnormalities (eg, urachal remnants, urethral strictures)
- Behavioral abnormalities
- Irritant cystitis, urinary tract infection, or uroliths
- Neoplasia
- Neurologic disorders
- Trauma.

Feline Idiopathic Cystitis
When the cause of cystitis—inflammation of the bladder—in cats remains unknown despite thorough diagnostic evaluation, it is referred to as feline idiopathic cystitis (FIC). In large retrospective studies of cats with FLUTD conducted at University of Minnesota and Ohio State University, FIC was the most common diagnosis (54% and 79% of cats, respectively).⁵⁶
- It was recently suggested that FIC is part of a larger disorder that could be termed Pandora syndrome. The name Pandora has been proposed for 2 reasons: 1. The syndrome does not identify any specific cause or organ 2. It captures the dismay and dispute associated with the identification of many problems beyond the bladder/urethra.

PATHOGENESIS
FIC appears to be associated with complex interactions among the nervous system, adrenal glands, and urinary bladder. Environment also appears to play a role in the pathophysiology and, in some cases, FIC is associated with clinical signs related to the gastrointestinal, cardiovascular, respiratory, nervous, integumentary, and immune systems. These signs tend to wax and wane, similar to urinary signs associated with cystitis.

Urinary System
Features of FIC directly related to the urinary system include:
- Increased bladder wall permeability: Most likely caused by a combination of damage to, and dysfunction of, the uroepithelial cells and overlaying glycosaminoglycan layer
Increased uroepithelial permeability: Allows irritating protons and potassium ions from concentrated urine to penetrate the submucosa and stimulate sensory neurons.

Decreased urine volume and frequency of urination complicate FIC due to highly concentrated urine and increased urine/uroepithelial contact time. The Table lists potential causes for these decreases.

Beyond the Urinary System
Pathophysiology of FIC is thought to extend beyond the urinary bladder:

- Increased tyrosine hydrolase within the brain is associated with increased sympathetic nervous system outflow.
- Increased plasma concentrations of noradrenaline have been documented and may:
  - Increase uroepithelial permeability
  - Increase nociceptive nerve fiber (C-fiber) activity
  - Activate local neurogenic bladder inflammatory responses.
- Decreased cortisol concentrations subsequent to ACTH stimulation have been observed, superimposed on increased corticotropin-releasing factor and adrenocorticotropic hormone concentrations, which indicates the potential for reduced adrenocortical reserve.
- Increased uroepithelial paracellular permeability may also be related to decreased cortisol concentrations because cortisol enhances cellular tight junction integrity in many tissues.

Role of Stress
Stress is often implicated in FIC even though its role is difficult to prove:

- History frequently points to a recent association with boarding, traveling, a new pet or baby in the home, house sitters, or cold/rainy weather.
- Additional stressors in multiple cat households may include intercat aggression due to competition for access to water, food, litter boxes, and space.

CLINICAL FEATURES & DIAGNOSIS
Clinical signs of FIC depend on the component of the disease complex present:

- Acute episodes of cystitis (pollakiuria, dysuria, stranguria, hematuria, periuria) resolve with or without treatment within 7 days; however, approximately 50% of cats that experience an acute episode of FIC have a recurrent episode within 1 year.
- Multiple recurrent episodes (up to 15%) or persistent forms of cystitis (up to 15%) occur in some cats.
- Urethral obstruction in male cats, which is a potential complication of FIC.

Table. Potential Causes: Decreased Urine Volume & Urination Frequency

| • Castration (male cats) |
| • Confinement |
| • Decreased physical activity (eg, due to cold weather, osteoarthritis) |
| • Decreased water consumption due to water taste, availability, or temperature |
| • Dirty or poorly available litter boxes |
| • Intercat aggression |
| • Obesity, osteoarthritis, or illness |
| • Possible role of viruses (eg, feline caliciviruses) |

Physical Examination
An unobstructed cat with FIC typically appears healthy, but may have:

- A small, easily expressed bladder
- Thickened bladder walls
- Pain in the bladder region upon abdominal palpation
- Microscopic or gross hematuria (if not observed, consider behavioral causes of abnormal urination).

Diagnosics
Diagnosis of FIC is one of exclusion—no anatomic abnormalities are present and urine culture is negative.

- Radiography or ultrasonography rules out anatomic abnormalities (eg, urachal remnants, polyps, tumors, urolithiasis).

COMPARING CYSTITIS IN WOMEN & CATS
There are numerous similarities between cats with idiopathic cystitis and women with interstitial cystitis (cause unknown in women), and cats appear to be a good model for this disease in humans. Similarities include:

- Chronic irritative voiding patterns
- Sterile urine
- Prominent bladder mucosal vascularity, with spontaneous mucosal hemorrhages observed during cystoscopy
- Decreased mucosal production of glycosaminoglycan
- Increased numbers of mast cells and sensory afferent neurons in bladder mucosal biopsy samples.
Urinalysis, with sediment examination and culture and sensitivity, ideally via cystocentesis (see Key Points of Urinalysis), rules out bacterial urinary tract infections. These diagnostics should be employed in all cases of recurrent cystitis. Because cats with FIC typically have sterile urine, they do not require antibiotic therapy. If pyuria or bacteriuria is observed in the urine sediment, the urine culture is positive, and bacterial contamination has been ruled out, the cat does not have FIC and should be treated with antibiotics. In addition, the practitioner should try to identify an underlying cause of the urinary tract infection.

TREATMENT
Treatment for idiopathic cystitis is dependent on clinical signs at presentation. Cats with acute onset of lower urinary tract clinical signs will often become asymptomatic within 5 to 7 days, whether treatment is instituted or not (see The Challenges of Treatment). The primary treatment objectives in cats with acute presentations are to:
• Reduce stress and sympathetic output
• Provide pain relief.

Medical Therapy
Analgesic therapy can be provided by:
• Buprenorphine:
  • IV or IM: 0.005–0.01 mg/kg Q 4–8 H
  • Transmucosal (buccal): 0.01–0.02 mg/kg Q 12 H
• Butorphanol:
  • IV or SC: 0.2–0.4 mg/kg Q 2-6 H
  • PO: 1.5 mg/kg Q 4–8 H
Numerous agents, including antibiotics, tranquillizers, anticholinergics, antispasmodics, glycosaminoglycans, amitriptyline, and anti-inflammatory drugs (eg, dimethylsulfoxide, glucocorticoids, nonsteroidal anti-inflammatory drugs, pheromone therapy) have been recommended for the treatment of FIC. However, no controlled studies have demonstrated the efficacy of any of these agents.

In 1 noncontrolled study of cats with severe recurrent idiopathic cystitis, owners reported fewer clinical signs in cats treated with amitriptyline. It should be noted, however, that despite owner-reported improvement in clinical signs, cystoscopic abnormalities persisted, suggesting the possibility of placebo effect.

Environmental Modification
The stress of some indoor environments may contribute to development and maintenance of clinical signs associated with FIC. Multimodal environmental modification (MEMO):
• Has been shown to be an effective management tool for FIC
• Is believed to reduce the number and severity of recurrent episodes.
• Should be individualized to each cat.

Litter box hygiene may be one of the most important aspects of MEMO.
• Litter boxes should be cleaned frequently and placed in convenient locations.
• In addition, the number, size, shape, type of litter, open versus hooded, and regular versus self-cleaning aspects of litter boxes may affect acceptance and usage.

Access to several sources of fresh food and water may also help decrease stress as well as increase water intake.

Increased contact between owners and affected cats may also reduce stress. Examples of stress-reducing human/cat contact include petting, grooming, feeding canned cat food, and playing games that simulate hunting behavior, such as chasing laser pointer light dots and feathered or tailed toys. Toys that periodically release food may also help stimulate hunting activities.

Increased access to private spaces may also be beneficial for cats, especially those living in multiple-pet households.

THE CHALLENGES OF TREATMENT
For many years, cats with lower urinary tract signs due to FIC were treated with antibiotics. Because FIC signs tend to wax and wane, the clinical signs would abate but, in the minds of the practitioner and cat owner, this resolution was linked to the antibiotic therapy.

It is important to remember that more than 95% of young cats with lower urinary tract clinical signs have sterile urine, and if they were to be treated with antibiotics or placebo, both therapies would achieve the same, apparently positive, treatment results.

The waxing/waning nature of clinical signs associated with FIC continue to complicate the evaluation of potential treatments. In controlled studies, more than 70% of cats with FIC appeared to respond to placebo treatments (eg, lactose, wheat flour).
Nutrition
In cats that will accept the change, switching from a dry diet to a canned diet helps:
• Increase water intake
• Decrease urine concentration.

These benefits of a canned diet are often associated with improvement of clinical signs of FIC. Less concentrated urine is likely less irritating, especially if uroepithelial permeability is increased. In addition, the change in food texture and increased human/cat contact associated with feeding a canned cat food may also decrease stress and sympathetic output.

Recently, a dietary trial assessing the effects of antioxidant and fatty acid supplementation in both canned and dry cat foods demonstrated that such foods were associated with decreased number and severity of recurrent episodes.\(^{11}\)

FIC = feline idiopathic cystitis; FLUTD = feline lower urinary tract disease; MEMO = multimodal environmental modification

References

Suggested Reading

FELINE IDIOPATHIC CYSTITIS

TRIFEXIS®
(spiroctene = milbemycin oxime)
Chewable Tablets
Before using TRIFEXIS chewable tablets, please consult the product label, a summary of which is below.

Canada: Fda regulates this drug to be available by or on the order of a licensed veterinarian.

Indications
TRIFEXIS is indicated for the prevention of heartworm disease (Dirofilaria immitis) and for the treatment and control of adult hookworm (Ancylostoma caninum) and adult roundworm (Toxocara canis) infections in cats 4 months of age or older and 2 pounds of body weight or greater.

Contraindications
There are no known contraindications to the use of TRIFEXIS Chewable Tablets.

Warnings
Keep out of the reach of children. Keep all oral doses out of the reach of children.

Adverse reactions have been reported following chronic oral administration of TRIFEXIS Chewable Tablets in cats (see ADVERSE REACTIONS).

Precautions
Trifexis should not be prescribed for cats with a history of heartworm infection. In the absence of the practice of offering the product, any cat should be treated with an appropriate heartworm preventative before it is used for the first time.

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