veterinary focus

#29.2

The worldwide journal for the companion animal veterinarian

2019 - $10 / 10€

CANINE AND FELINE URINARY DISEASE

ROYAL CANIN®

URINE AND TAXATION – AN UNUSUAL COMBINATION?

"Rem tene; verba sequentur" **— Cato the Elder**

Ancient Rome gave our modern world many things – for example, concrete, underfloor heating, sewers and drainage – and we can all name some of the emperors that ruled this early civilization. Nero, Caesar and Augustus will be familiar to most of us, but the emperor Vespasian (who reigned between AD 69-79) is less well known – yet he is still noteworthy. Not only did he reform Rome's financial system and initiate several ambitious construction projects (including the Colosseum), he was the person who enforced a urine tax to raise government funds. Which, incidentally, is why a public urinal in France is sometimes called a "vespasienne".

An unusual tax, one might think, but it was introduced because urine had a value. Ancient Romans would urinate into pots, and the liquid was then collected and sold, as it was an essential ingredient used in several chemical processes. Not only was it an excellent agent for cleaning and whitening togas, it was indispensable for leather tanning – and so the buyers of the urine, however reluctantly, paid the tax for it.

Leather tanning has moved on since then, and togas are less plentiful, but the wisdom from ancient Romans remains. The Latin quotation above, from a Roman senator, translates as "Grasp the subject, the words will follow" and we believe that this issue of *Veterinary Focus* does indeed go to the heart of the matter under review, so that the reader should find that urinary disorders in general are a little bit less taxing.

Ewan McNEILL
Editor-in-chief

• Focus on *Veterinary Focus*

What's in a name? More than one might think in many cases, and especially when it comes to the nomenclature used for various manifestations of urinary bladder disease. **Using the correct terminology** can be invaluable in the classification and management of such conditions.

p02

Recent advances offer innovative alternatives to the traditional surgical approach for removing uroliths; these minimally invasive options are changing the way we tackle this commonly encountered clinical problem.

p09

p16

Canine urinary incontinence can be both a challenge to diagnose and a frustration to treat, as the possible causes are various and the potential treatments are not guaranteed to work in every case.

veterinary focus #29.2

PEFC 10-31-1668

Origine du papier : VIRTON (Belgique)
Taux de fibres recyclés : 0%
Certification : 100% PEFC
Impact sur l'eau : 0.012 P tot kg/tonne

Deputy publisher: Buena Media Plus
Bernardo Gallitelli 90, rue de Paris
92100 Boulogne-Billancourt, France
Phone: +33 (0) 1 72 44 62 00

Editor-in-chief: Ewan McNeill, BVMS, Cert VR, MRCVS
Editorial secretary
- Laurent Cathalan (lcathalan@buena-media.fr)

Artwork
- Audrey Barbutti

Printed in the European Union
ISSN 2430-7874

Legal deposit: June 2019
Cover: Shutterstock

Veterinary Focus is published in Brazilian Portuguese, Chinese, English, French, German, Italian, Japanese, Polish, Russian, Spanish and Korean.

Find the most recent issues on: http://vetfocus.royalcanin.com and www.ivis.org.

DEFINING AND MANAGING CANINE URINARY INFECTIONS

Terminology can be important when dealing with canine urinary problems, as it facilitates clear understanding of the disease process and assists in decision-making for both diagnosis and treatment, as J. Scott Weese describes.

KEY POINTS

1. Urinary tract disease is a common and potentially problematic condition; how the condition is defined can help in the decision-making process for diagnosis and treatment.
2. The urinary bladder was previously considered a sterile site but it is now thought that bacteria may cycle in and out of the bladder on a routine basis.
3. Dogs with recurrent urinary tract disease can be difficult and frustrating to manage, and it is essential to determine why this is happening to achieve long-term clinical success.
4. It is now generally recognized that subclinical bacteriuria in dogs does not usually need to be treated.

Introduction

Urinary tract disease is a common problem in dogs and a leading reason for antimicrobial use. In addition to patient welfare issues, infections can be problematic because of cost, owner frustration and the potential for complications (*e.g.*, struvite urolithiasis). These problems are compounded in dogs with recurrent or poorly responsive infections.

Because of the importance of urinary tract disease in dogs, clinical guidelines have been produced by the International Society for Companion Animal Infectious Diseases (ISCAID), describing diagnosis, treatment and prevention recommendations (1). The size and scope of the guidelines demonstrate the potential complexity of urinary tract disease in dogs and offer valuable advice to clinicians.

What's in a name?

Terminology can be important, as it facilitates clear understanding and communication of the disease process. This can play a role in decision-making regarding diagnosis or treatment. A variety of different classifications or descriptions can be used **(Table 1)**.

Urinary tract infection vs. bacterial cystitis

"Urinary tract infection" or "UTI" is common nomenclature; however, this term is used variably in the veterinary literature, including situations where lower urinary tract disease is present (2,3), as well as cases where there are no overt signs of disease but bacteria are detected by culture or cytological examination of the sediment (4-7). This can cause confusion regarding the clinical relevance of results if cystitis is not differentiated from subclinical bacteriuria, as discussed below.

Because of the potential confusion revolving around "urinary tract infection", the variability in how the term is used, and a need to focus on the disease process (*e.g.*, cystitis), it has been recommended to use the term "bacterial cystitis" when referring to bacterial infection of the lower urinary tract that results in evidence of disease (1).

Subclinical bacteriuria

Traditionally, the urinary bladder has been considered to be essentially a sterile site. However, it is now apparent that this is not the case. Bacteria likely cycle in and out of the bladder on a routine basis, with this being more common in female dogs (because of the short urethra) and in certain diseased populations (*e.g.*, animals that are immunosuppressed, have spinal cord disease, or are morbidly obese). Apart from movement of

J. Scott Weese,

DVM, DVSc, Dipl. ACVIM, Ontario Veterinary College, University of Guelph, ON, Canada

J. Scott Weese is currently Professor at the Ontario Veterinary College and a Zoonotic Disease/Public health Microbiologist at the University of Guelph's Centre for Public Health and Zoonoses. The author or co-author of over 200 papers in peer-reviewed journals, he has edited two textbooks and is frequently invited to speak on infectious disease topics. His research interests include microbiome assessment, antimicrobial resistance and infection control.

single organisms in and out of the bladder, there is increasing information suggesting that a "urine microbiota" is present. This has not been reported in dogs, but human studies using advanced techniques have identified a variable microbial population in the urine of healthy individuals, as well as people with medical conditions such as spinal cord disease and renal disease (8-10). While much less abundant and diverse than sites such as the gastrointestinal tract, a large number of different bacteria can be identified. The dynamics of the microbiota, its role in disease and even whether viable bacteria (rather than just DNA) are present remain to be elucidated.

Table 1. Quick reference definitions.

Urinary tract infection	A term that can cause confusion as it is sometimes used to indicate disease or subclinical bacteriuria
Bacteriuria	The presence of bacteria in the urine
Bacterial cystitis	A more precise term that indicates the presence of bladder inflammation from bacterial infection
Recurrent cystitis	Bacterial cystitis that has occurred 3 or more times in the preceding year
Refractory cystitis	Bacterial cystitis that has not responded to appropriate treatment
Persistent infection	Clinical recurrence of cystitis with what is potentially the same organism, suggesting failure to eliminate the bacterium
Reinfection	Clinical recurrence of cystitis that follows successful elimination of the original organism, often detected by identification of a different bacterial species in a subsequent culture
Subclinical bacteriuria	The presence of bacteria in urine in the absence of signs of lower urinary tract disease
Uncomplicated	A term used in human medicine for infections that typically occur in young, sexually active women without other evident risk factors or abnormalities. This may not be analogous to the types of cases typically seen in canine patients, as it is questionable whether truly "uncomplicated" cases occur; use of the term is discouraged
Complicated	A term that has been used to describe recurrent infections or infections in hosts with comorbidities or other complications (*e.g.*, endocrinopathy). However, this is a broad group and designation as "complicated" does little in itself to inform diagnostic or treatment decisions

Irrespective of whether bacteria are in the bladder as a sporadic transient event or as part of an overlooked resident microbiota, it is clear that bacteria are commonly found in the canine bladder without evidence of lower urinary tract disease. Prevalence varies by study and dog population, but can be high **(Table 2)**.

One shift in the approach to urinary tract disease in dogs has been recognition that subclinical bacteriuria does not usually need to be treated (1). In humans, substantial efforts are undertaken to reduce treatment of subclinical bacteriuria because of a lack of evidence of need and concerns about antimicrobial resistance (11-15). Treatment of subclinical bacteriuria has been associated with increased risk of subsequent UTI in healthy women, when compared to untreated controls (16). Concern is sometimes expressed about the potential for subclinical bacteriuria to progress to cystitis, pyelonephritis or urosepsis. However, data indicating a risk are lacking in dogs. Study has been limited, but bacteriuria was not associated with outcome in paralyzed dogs (17) or otherwise healthy female dogs (18). Further, when one considers the potentially high prevalence of subclinical bacteriuria in some dog populations (*e.g.*, diabetics, obese dogs, dogs on immunosuppressive medications) and the low incidence of urinary tract disease or urosepsis

Table 2. Reported prevalences of subclinical bacteriuria in dogs.

Population	Bacteriuria prevalence
Elective surgical patients (19)	2.1%
Ciclosporin treated dogs (20)	30%
Glucocorticoid treated (21)	18%
Hyperadrenocorticism (22)	46%
Diabetics (22)	37%
Puppies with parvoviral enteritis (23)	26%
Healthy puppies (23)	6.3%
Morbidly obese (24)	13%
Oclacitinib treated (25)	3%

in those populations, the notion that subclinical bacteriuria is typically a benign state becomes apparent. Therefore, treatment of subclinical bacteriuria is not usually recommended (26).

Complicated or uncomplicated, or does it matter?

Classification of bacterial cystitis in dogs has often used human terminology; "simple uncomplicated" or "complicated". However, it is unclear whether those definitions are applicable. At best, they are an over-simplification of the range of infections that occur. At worst, they are inaccurate and potentially misleading. In humans, "simple uncomplicated" UTI typically refers to sporadic infections in otherwise healthy women with no apparent risk factors apart from sexual activity and no underlying factors that would increase the risk of treatment failure. Most of these infections are in healthy, sexually active young women, a population without a direct analogy to most dogs. That does not mean that uncomplicated infections do not occur in dogs. Rather, what actually constitutes an uncomplicated infection and how (or if) that alters management is unclear. Defining a dog as having a "complicated" infection often leads to automatic recommendation of longer durations (*e.g.*, 28 days) of antimicrobials, something that may not always (or often) be warranted. Even within complicated cases, the approach must vary. For example, a dog with recurrent infections caused by an anatomical abnormality may be more akin to having a series of "uncomplicated" infections that respond to short duration treatment. Therefore, in the author's opinion, "complicated" and "uncomplicated" terminology is best avoided as it may lead to unnecessary assumptions or approaches.

Does persistent infection vs. re-infection matter?

In a word, yes. Patients with recurrent disease can be difficult and frustrating to manage. When infections recur, determining the reason is critical to have any potential for long-term clinical success. Repeated antimicrobial treatment in lieu of determining the root of the problem is a suboptimal approach that can result in repeated disease and increasingly resistant infections from repeated antimicrobial exposure. Ultimately, a cause cannot be identified in all patients with repeated infections, and when a cause is identified, it is not always treatable. However, it is worthwhile to attempt to identify the underlying cause.

Determining whether infections are likely because of a failure to eliminate the offending organism (persistent infection) or because of repeated entry of new organisms into the bladder (re-infection) will alter the approach to diagnosis and management.

Can we differentiate persistent vs. repeated new infections?

The short answer is – sometimes. If different bacterial species are identified each time, then re-infection is obvious. If the same bacterial species is present but it has a markedly different susceptibility profile (especially differences in resistance that are based on acquisition or loss of a gene, such as beta-lactam resistance), then re-infection is likely. If the same bacterial species with the antimicrobial susceptibility is identified, this could represent persistent infection or it could be re-infection with a similar strain, something that can only be discerned through molecular typing. Determining which of these scenarios is most likely can refine the list of leading differential diagnoses and streamline the diagnostic plan **(Table 3)**.

Diagnosis of bacterial cystitis

In dogs, strong suspicion of bacterial cystitis can be generated based on history and physical examination. In contrast to cats, where most cases of lower urinary tract disease do not have an infectious cause, bacterial cystitis can reasonably be suspected in dogs with typical clinical signs (*e.g.*, pollakiuria, stranguria, hematuria and/or dysuria in the absence of extra-urinary signs). Urinalysis should be performed since it is an easy, cost-

Table 3. Potential causes and approaches to recurrent bacterial cystitis.

Persistent infection	
Possible causes	**Possible approaches**
Poor owner compliance	Discussion with owner about compliance.
Falsely reported antimicrobial susceptibility	Review of culture results, drug choice and prescribed regimen
Improper drug selection	
Improper dosing regimen	
Nidus where the bacterium can evade antimicrobials (*e.g.*, urolith, mass)	Diagnostic imaging
Invasion of bladder wall (especially if a drug with lesser tissue activity, *e.g.*, amoxicillin, was used)	Cystoscopy
Prostatitis	

Re-infection	
Possible causes	**Possible approaches**
Anatomical abnormality (congenital or acquired, such as via obesity)	Reproductive examination
Immunocompromise (disease or drug, including endocrinopathies)	Hematology
Renal disease (*e.g.*, low urine specific gravity)	Diagnostic imaging and cystoscopy

Figure 1. Urinalysis should be performed – wherever possible – in any dog presenting with signs of a possible urinary infection, as it is an easy, cost-effective and useful diagnostic step.

Figure 2. Urine cytology from a dog with bacterial cystitis. Note the white blood cells (solid arrow) and red blood cells (dashed arrow).

effective and useful diagnostic step **(Figure 1)**. Urine specific gravity (USG) can provide information about renal function. Dipstick analysis can identify or confirm hematuria, provide information about urine pH and identify potentially relevant abnormalities such as glucosuria. Cytology can help confirm a diagnosis through detection of white blood cells, red blood cells and bacteria, and may identify crystals, casts or abnormal cells that might indicate concerns about urolithiasis, renal disease or bladder neoplasia, respectively **(Figure 2)**.

Whilst urine culture is preferred, empirical therapy is justifiable in dogs with a first episode of bacterial cystitis. Culture is not usually needed to confirm the diagnosis, so it is most relevant for choosing the antimicrobial. In situations where resistance to first-line options is unlikely (*e.g.*, a dog has not had recent antibiotic treatment and the prevalence of resistance in the area is low), there is a high chance of success with empirical therapy. When the likelihood that a resistant pathogen is present increases, either because of dog or population factors, culture becomes more important. Free-flow samples are fine for cytology but cystocentesis is preferred for culture. It has been shown that cleanly collected free-flow samples can provide similar results to cystocentesis when samples can be processed by the laboratory within hours and when a cut-off of 100,000 CFU/mL is used (27). The inherent delay from sample collection to processing by the laboratory precludes this as a viable option in most clinical situations, unless in-house culture is performed. Therefore cystocentesis should be considered the default technique when culture is desired.

It is important to critically interpret culture results, even when cystocentesis samples are used. Contamination and colonization can result in isolation of bacteria that are not clinically relevant. Whenever multiple organisms are identified, thought should be put into which is the most likely offending agent, as targeting of all of the bacteria may not be required. When bacteria that are not usually uropathogens are identified (*e.g.*, *Bacillus*, coagulase negative *Staphylococci*, various environmental organisms), it is important to consider whether they might be contaminants. Pure growth of an uncommon organism might truly indicate infection by that organism, so it cannot be completely dismissed. However, this is not guaranteed, and use of higher tier drugs for multidrug resistant but clinically questionable bacteria may not be required, and empirical treatment with typical first-line options may be preferable, despite contradictory culture results.

There should be some consideration of underlying causes, as most cases probably have some inciting (if not elusive) cause. Detailed investigation after a single episode is hard to justify, but investigation is never contraindicated, and is certainly indicated when recurrent disease is present **(Figure 3)**.

Treatment of bacterial cystitis

There has been a marked shift in the approach to bacterial cystitis in dogs in the past decade. While long (*e.g.*, 14 day) durations were widely used, this was done without evidence of optimal durations. In humans, shorter periods (*e.g.*, 3-5 days) are typically recommended (28,29), with little reason to believe that there should be a difference for dogs. The 2011 ISCAID guidelines recommended 7-10 days of treatment, with a comment that shorter durations are probably effective, but evidence is lacking (26). Subsequently, studies have reported comparable efficacy of shorter durations as compared to typical longer durations in dogs, such as clinical equivalency of three days of trimethoprim-sulfa compared to 10 days of cephalexin (3), or three days of enrofloxacin compared to 14 days of amoxicillin/clavulanic acid (2). Randomized controlled studies comparing outcomes after use of the same drug for different durations are still lacking, but evidence to date supports use of shorter treatment regimens

© Dr. Michelle Evason

Figure 3. Persistent infection in the bladder can be due to the presence of a nidus where the bacterium can evade antimicrobials, such as uroliths.

than in the past. As such, the revised 2019 ISCAID guidelines recommend 3-5 days of treatment for sporadic cystitis (1). First-line antimicrobial options are presented in **Table 4**. Other antimicrobials may be indicated in some cases based on antimicrobial susceptibility, disease aspects (*e.g.*, concern about involvement of tissue, not just urine and uroepithelium), patient drug tolerance and owner compliance with dosing regimens.

Case studies

Many of the above points can be covered by illustration of a few cases studies.

Case study 1 – Subclinical bacteriuria

Meg is an 8-year-old Golden Retriever who was identified as bacteriuric from culture of a cystocentesis sample collected at an annual wellness visit. She did not have signs of lower urinary tract disease. She has a history of inflammatory bowel disease that has been controlled on a low dose (5 mg q24h) of prednisone. Bacteriuria (> 40/hpf) was evident microscopically, with mild pyuria (5-10 WBC/hpf) but no hematuria. USG was 1.044. Hematology was unremarkable. She was diagnosed with subclinical bacteriuria and treatment was not recommended.

While routine clinical testing of dogs without evidence of lower urinary tract disease is not typically recommended (1), Meg has been followed with serial urinalyses to better understand this disease. Urine samples have been collected, typically on a monthly basis. Cystocentesis has been performed when possible; otherwise, free-flow samples have been collected and processed within hours and using a cut-off of > 100,000 CFU/mL (27). *E. coli* has been isolated from every urine sample over the past 8 months. An inflammatory sediment has been identified, with white blood cells but no gross or microscopic hematuria. No signs of urinary tract disease (or any other disease) have been noted. Since she has had no evidence of disease, treatment has not been recommended and no problems have been encountered. The reason for subclinical bacteriuria has not been identified, and cystoscopy would be the next diagnostic step.

Meg is an example of persistent subclinical bacteriuria. In the past, each of these episodes where *E. coli* was isolated would likely have led to antimicrobial treatment. However, in humans, abundant data indicate that treatment of people with bacteriuria in the absence of clinical signs is not rewarding. Widespread efforts are ongoing in human medicine to reduce testing and treatment of people with subclinical bacteriuria. This includes patients with complex medical histories (*e.g.*, renal transplant recipients and people that cannot report clinical signs, such as paralyzed individuals and those with dementia). Therefore, since Meg is not suffering any apparent problems from this bacterium, she is not being treated.

Case study 2 – Sporadic bacterial cystitis

Molly is a 4-year-old Labradoodle who is presented with pollakiuria and dysuria of 24 hours duration. Molly is otherwise healthy, with an unremarkable medical history and physical examination. A free-flow urine sample is collected which is grossly abnormal; cloudy and red-tinged with flocculent material. Dipstick results indicate hematuria but no other abnormalities. USG is 1.030, and cytology is consistent with cystitis, with 50 RBC and 20-30 WBC/hpf. Numerous rod-shaped bacteria are evident, and bacterial cystitis is the most likely cause. Furthermore, in a dog with no recent antimicrobial exposure or hospitalization, the odds of a resistant infection are deemed very low. Given those factors, cystocentesis and culture are discussed with the owner but are not strongly recommended. The owner elects to forego culture. Amoxicillin (20 mg/kg PO q12h for 4 days) is prescribed. A single dose of meloxicam (0.2 mg/kg PO) is also administered to help control pain. Clinical signs improve within 24h. A follow-up telephone call a few days after cessation of antimicrobials is performed and the owner reports no problems. No further signs of lower urinary tract disease are reported at Molly's next wellness visit, six months later.

While rather simplistic, this case shows a typical scenario. Culture is a useful tool but is less rewarding when it is of little use for making the diagnosis (bacterial cystitis) and when the odds of resistance to typical empirical antimicrobials are low. This is the case in most dogs with sporadic bacterial cystitis and no history of antimicrobial exposure or hospitalization. However, culture is never contraindicated and would have been desirable had treatment failed, so discussion of the cost-benefit of culture is warranted in any dog with suspected bacterial cystitis.

Case study 3 – Struvite urolithiasis

Frankie is an 8-year-old mixed breed neutered male dog that is presented for pollakiuria and stranguria of at least 14 days duration. Physical examination is unremarkable and he has no history of previous urinary tract infections.

"If active bacterial cystitis which is secondary to a urolith is under control, there is no evidence that further antimicrobial treatment is needed if medical dissolution of the urolith is being pursued."

J. Scott Weese

Because sporadic bacterial cystitis is less common in adult male dogs, a cystocentesis sample is collected for urinalysis and culture. Urine pH is 8 and USG is 1.028. Hematuria (100 RBC/hpf) is evident, with mild pyuria (10 WBC/hpf). Sporadic cocci are noted, along with moderate numbers of struvite crystals. Because of concern about struvite urolithiasis, based on the crystalluria, cocci and high urine pH, abdominal radiographs are taken. A urolith consistent with struvite urolithiasis is identified. Options are discussed and the owner elects to attempt medical treatment.

Empirical treatment with amoxicillin (20 mg/kg PO q12h) is chosen, for a duration of 7 days. The longer duration compared to Meg is because of the complicating factor of the urolith, which could potentially result in more inflammation of the bladder wall and a more complicated local environment. However, once the active cystitis is controlled, there is no evidence that antimicrobials are needed if medical dissolution of the urolith is being pursued (1). While some clinicians use antimicrobials throughout the dissolution period, supporting data are not available. Data indicating efficacy without antimicrobials are similarly lacking; however, anecdotal information from clinicians that do not use antimicrobials during dissolution, with good success, supports a conservative approach to antimicrobials. Once the active infection is eliminated, it is difficult to justify ongoing treatment since no clinically relevant bacteria should be

Table 4. First-line recommendations for treatment of sporadic bacterial cystitis*.

Drug and dosing regime	Comments
Amoxicillin 11-15 mg/kg PO q8-12h	Ideal first-line option. Excreted in high concentrations in urine. Urine specific breakpoints should be used because some bacteria that are deemed resistant based on serum levels are susceptible in urine.
Amoxicillin-clavulanic acid 12.5-25 mg/kg PO q12h	Unclear whether clavulanic acid confers much advantage in urine over amoxicillin alone, as high amoxicillin levels are achieved in urine.
Trimethoprim-sulfonamide 15-30 mg/kg PO q12h	Many useful aspects make it a first-line option, but adverse effect risks usually relegate it to a "1b" choice, when amoxicillin and amoxicillin/clavulanic acid are not options.

* Clinicians should bear in mind national guidelines for antibiotic usage wherever appropriate.

present. The potential for liberation of bacteria embedded in the urolith as it dissolves is often discussed; however, while bacteria can be found within uroliths, there is no evidence that adequate numbers of viable bacteria are eliminated to cause subsequent infections.

Culture results are obtained on day 4 and *Staphylococcus pseudintermedius*, > 100,000 CFU/mL, is reported. The bacterium is susceptible to amoxicillin and the lower urinary tract signs resolve quickly. A dissolution diet is prescribed and the urolith is no longer evident radiographically 8 weeks later. No further episodes of urinary tract disease are encountered over the next year.

CONCLUSION

The terminology employed when classifying urinary tract disease is important, because it allows better understanding of the disease process and assists communication, both between the owner and the clinician, and between members of the veterinary care team. When the correct terminology is used it can, in turn, play a useful part in decision-making regarding diagnosis or treatment for dogs with urinary tract signs. Further research into the role of urinary bacteria will allow better understanding of canine bladder disease pathophysiology.

REFERENCES

1. Weese JS, Blondeau J, Boothe D, *et al*. International Society for Companion Animal Infectious Diseases (ISCAID) guidelines for the diagnosis and management of bacterial urinary tract infections in dogs and cats. *Vet J* in press.
2. Westropp JL, Sykes JE, Irom S, *et al*. Evaluation of the efficacy and safety of high dose short duration enrofloxacin treatment regimen for uncomplicated urinary tract infections in dogs. *J Vet Intern Med* 2012;26:506-512.
3. Clare S, Hartmann FA, Jooss M, *et al*. Short- and long-term cure rates of short-duration trimethoprim-sulfamethoxazole treatment in female dogs with uncomplicated bacterial cystitis. *J Vet Intern Med* 2014;28:818-826.
4. Bubenik L, Hosgood G. Urinary tract infection in dogs with thoracolumbar intervertebral disc herniation and urinary bladder dysfunction managed by manual expression, indwelling catheterization or intermittent catheterization. *Vet Surg* 2008;37:791-800.
5. Bubenik LJ, Hosgood GL, Waldron DR, *et al*. Frequency of urinary tract infection in catheterized dogs and comparison of bacterial culture and susceptibility testing results for catheterized and non-catheterized dogs with urinary tract infections. *J Am Vet Med Assoc* 2007;231:893-899.
6. Lusby AL, Kirk CAB, Moyers TD, *et al*. Prevalence of asymptomatic bacterial urinary tract infections in morbidly obese dogs. *ACVIM Forum* 2011.
7. Olby NJ, MacKillop E, Cerda-Gonzalez S, *et al*. Prevalence of urinary tract infection in dogs after surgery for thoracolumbar intervertebral disc extrusion. *J Vet Intern Med* 2010;24:1106-1111.
8. Kramer H, Kuffel G, Thomas-White K, *et al*. Diversity of the midstream urine microbiome in adults with chronic kidney disease. *Int J Urol Nephrol* 2018;50:1123-1130.
9. Siddiqui H, Nederbragt AJ, Lagesen K, *et al*. Assessing diversity of the female urine microbiota by high throughput sequencing of 16S rDNA amplicons. *BMC microbiology* 2011;11:244.
10. Fouts DE, Pieper R, Szpakowski S, *et al*. Integrated next-generation sequencing of 16S rDNA and metaproteomics differentiate the healthy urine microbiome from asymptomatic bacteriuria in neuropathic bladder associated with spinal cord injury. *J Transl Med* 2012;10:174.
11. Harding GKM, Zhanel GG, Nicolle LE, *et al*. Manitoba Diabetic Urinary Infection Study Group. Antimicrobial treatment in diabetic women with asymptomatic bacteriuria. *N Engl J Med* 2002;347:1576-1583.
12. Cai T, Mazzoli S, Mondaini N, *et al*. The role of asymptomatic bacteriuria in young women with recurrent urinary tract infections: to treat or not to treat. *Clin Infect Dis* 2012;55:771-777.
13. Leis JA, Rebick GW, Daneman N, *et al*. Reducing antimicrobial therapy for asymptomatic bacteriuria among non-catheterized inpatients: A proof-of-concept study. *Clin Infect Dis* 2014;58:980-983.
14. Naik AD, Trautner BW. Editorial commentary: doing the right thing for asymptomatic bacteriuria: knowing less leads to doing less. *Clin Infect Dis* 2014;58:984-985.
15. Nicolle LE, Bradley S, Colgan R, *et al*. Infectious Diseases Society of America guidelines for the diagnosis and treatment of asymptomatic bacteriuria in adults. *Clin Infect Dis* 2005; 40:643-654.
16. Cai T, Nesi G, Mazzoli S, *et al*. Asymptomatic bacteriuria treatment is associated with a higher prevalence of antibiotic resistant strains in women with urinary tract infections. *Clin Infect Dis* 2015;61:1655-1661.
17. Rafatpanah Baigi S, Vaden S, Olby NJ. The frequency and clinical implications of bacteriuria in chronically paralyzed dogs. *J Vet Intern Med* 2017;31:1790-1795.
18. Wan SY, Hartmann FA, Jooss MK, *et al*. Prevalence and clinical outcome of subclinical bacteriuria in female dogs. *J Am Vet Med Assoc* 2014;245:106-112.
19. McGhie JA, Stayt J, Hosgood GL. Prevalence of bacteriuria in dogs without clinical signs of urinary tract infection presenting for elective surgical procedures. *Aust Vet J* 2014 92:33-37.
20. Peterson AL, Torres SM, Rendahl A, *et al*. Frequency of urinary tract infection in dogs with inflammatory skin disorders treated with ciclosporin alone or in combination with glucocorticoid therapy: a retrospective study. *Vet Dermatol* 2012;23:201-e43.
21. Torres SMF, Diaz SF, Nogueira SA, *et al*. Frequency of urinary tract infection among dogs with pruritic disorders receiving long-term glucocorticoid treatment. *J Am Vet Med Assoc* 2005;227:239-243.
22. Forrester SD, Troy GC, Dalton MN, *et al*. Retrospective evaluation of urinary tract infection in 42 dogs with hyperadrenocorticism or diabetes mellitus or both. *J Vet Intern Med* 1999;13:557-560.
23. Koutinas AF, Heliadis N, Saridomichelakis MN, *et al*. Asymptomatic bacteriuria in puppies with canine parvovirus infection: a cohort study. *Vet Microbiol* 1998;63:109-116.
24. Wynn SG, Witzel AL, Bartges JW, *et al*. Prevalence of asymptomatic urinary tract infections in morbidly obese dogs. *Peer J* 2016;4:e1711.
25. Simpson AC, Schissler JR, Rosychuk RAW, *et al*. The frequency of urinary tract infection and subclinical bacteriuria in dogs with allergic dermatitis treated with oclacitinib: a prospective study. *Vet Dermatol* 2017;28:485-e113.
26. Weese JS, Blondeau J, Boothe D, *et al*. Antimicrobial use guidelines for treatment of urinary tract infections in dogs and cats: antimicrobial guidelines working group of the International Society for Companion Animal Infectious Diseases. *Vet Med Int* 2011;4:1-9.
27. Sorensen TM, Jensen AB, Damborg P, *et al*. Evaluation of different sampling methods and criteria for diagnosing canine urinary tract infection by quantitative bacterial culture. *Vet J* 2016;216:168-173.
28. Gupta K, Hooton TM, Naber KG, *et al*. International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: A 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. *Clin Infect Dis* 2011;52:e103-20.
29. Warren JW, Abrutyn E, Hebel JR, *et al*. Guidelines for antimicrobial treatment of uncomplicated acute bacterial cystitis and acute pyelonephritis in women. Infectious Diseases Society of America (IDSA) 1999;29:745-758.

MINIMALLY INVASIVE BLADDER UROLITH REMOVAL

Minimally invasive options for removal of uroliths are now the standard of care in human medicine, and similar methods are finding increasing application in veterinary medicine, as Marilyn Dunn describes.

Marilyn Dunn,

DMV, MVSc, Dipl. ACVIM, Centre Hospitalier Universitaire Vétérinaire, University of Montreal, Quebec, Canada

Marilyn Dunn is currently a professor in internal medicine and heads the interventional medicine service at the University of Montreal. A graduate of the University, she was board certified by the ACVIM in 1999 and is a founding member (and current president) of the Veterinary Interventional Radiology and Interventional Endoscopy Society (VIRIES). Her main interests are in urinary tract and respiratory interventions, and thrombosis management. She has published many scientific articles and book chapters, and lectures widely on interventional medicine.

KEY POINTS

1. Uroliths should always be removed from the urinary tract in the least invasive manner possible.
2. Struvite uroliths in cats and dogs can be dissolved within a short time period, and dissolution should be considered before more interventional techniques.
3. The minimally invasive technique chosen is tailored for an individual patient based on its size and gender, as well as the number and size of the stones.
4. Urolith analysis is essential in order to instigate proper preventative measures to reduce urolith recurrence.

Introduction

Lower urinary tract stones, not amenable to medical dissolution, can be removed through various minimally invasive methods. Stone removal is generally recommended as their continued presence can induce inflammation, obstruction or recurrent infection. Surgical removal of uroliths by cystotomy or urethrotomy has been the traditional method of choice, but both techniques have been associated with various complications – including urine leakage, wound dehiscence, bleeding, stricture formation and incomplete stone removal – reported in 20% of canine patients (1). Additionally, suture material within the urethra or bladder wall may serve as a nidus for future urolith formation in stone-forming patients; analysis of recurrent lower urinary tract stones in patients that had undergone surgical cystotomy determined that 9.4% were suture-induced (2). Recently, complications associated with traditional surgical cystotomy, regardless of closure method, were reported in 37-50% of cases, with a mean duration of hospitalization of 4 days (3).

In humans, minimally invasive treatment options have mostly replaced traditional surgical stone removal, as this is associated with a high recurrence rate of calculi, the need for serial surgeries that can lead to suture-induced stones, strictures, adhesions, bleeding, uroabdomen, pain and other life-threatening complications (4,5). The current standard of care for human urinary tract stones that cannot be passed or medically dissolved typically involves the use of minimally invasive methods.

Such approaches have a multitude of advantages over standard surgery, including shorter hospitalization times, little to no recovery time and less discomfort. In small animals, minimally invasive treatment options for lower urinary tract stones consist of voiding urohydropropulsion (VUH), cystoscopic stone basket retrieval, intracorporeal lithotripsy and percutaneous cystolithotomy (PCCL) **(Figure 1)**.

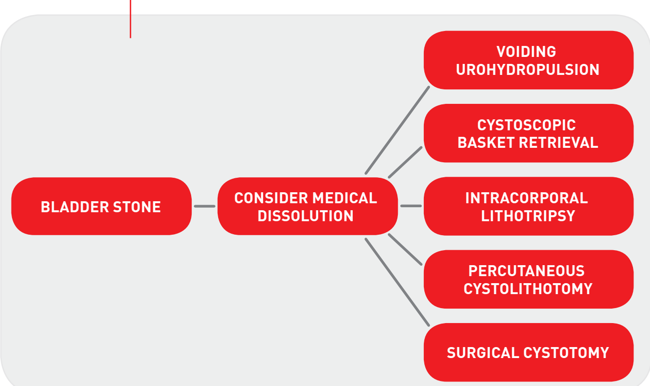
Minimally invasive removal options should be considered, discussed and offered to owners of pets suffering from uroliths (6). While at times appearing technically simple, these procedures have been associated with serious complications when performed by inadequately trained personnel, and referral to a formally trained and experienced specialist is indicated.

This article will review the current minimally invasive treatment options for bladder and urethral urolith removal. All the procedures described below should be performed in a sterile manner, with patients clipped and aseptically prepared, and all instruments which will enter the urinary tract must be sterile.

Bladder and urethral urolithiasis

Various interventional approaches may be considered for removal of lower urinary tract uroliths, depending on the species, sex, type of stone present and stone burden, and consideration of a minimally invasive approach to stone removal in lieu of surgical cystotomy is to be recommended in most cases. Correct assessment of stone size is critical in selecting the most appropriate intervention. Uroliths should be measured by standard radiography (or contrast radiography for radiolucent stones) using a radiopaque marker, rather than by ultrasound, which tends to overestimate urolith size and underestimate the number of uroliths (6).

Figure 1. A simple algorithm for the recommended approach to bladder urolith removal.



Voiding urohydropropulsion

Indications

This method **(Box 1)** allows antegrade removal of bladder stones through the urethra. It is recommended for small stones < 3-4 mm diameter in female dogs, < 2.5 mm in female cats, but is limited by the size of the penile urethra in male dogs. Voiding urohydropulsion should not be attempted in male cats, as there is a high risk of urethral obstruction (7).

Equipment

An appropriately sized urinary catheter, syringe, and saline.

Intervention

Under general anesthesia, a urinary catheter is used to fill the bladder with saline. It is important to avoid overfilling; the estimated bladder capacity is 10-15 mL/kg. If a urinary catheter cannot be passed in a female dog or cat, the catheter can be inserted into the vestibule and the vulva gently closed with digital pressure; filling of the vestibule with saline will result in passive filling of the vagina, urethra and bladder. The bladder should be palpated during filling to avoid over-distension, and filling should be stopped when it feels firm. The urinary catheter is then removed; in females, the patient is then positioned vertically, males are placed in lateral recumbency. The urinary bladder is palpated, shaken gently and pulled cranially to straighten the urethra. Gentle but steady pressure is applied to the urinary bladder to induce micturition. The procedure is repeated until all stones have been retrieved **(Figure 2)**.

Box 1. At a glance... Voiding urohydropropulsion.

Size and number of uroliths	Stones < 3-4 mm in small female dogs
	Stones < 2.5 mm in female cats
	Male dogs limited by size of penile urethra
Sex and species	Female dogs and cats
	Not indicated in male cats as risk of urethral obstruction
Advantages	Quick
	Low-cost equipment
	Can be done in general practice
Disadvantages	Stones may remain in the bladder
	Large and spiculated stones may obstruct the urethra

© Marilyn Dunn

Figure 2. An anesthetized cat has had its bladder filled with saline following urethral catheterization. The cat is held vertically and the bladder palpated **(a)**. The bladder is then pulled cranially and gently compressed to generate a urine stream **(b)**.

Complications

This procedure is generally well tolerated, but mild hematuria may be noted. Careful palpation of the urinary bladder while filling with saline is recommended in order to prevent overfilling and bladder rupture. Inadvertent urethral obstruction due to numerous uroliths being voided may occur while performing the procedure.

Alternatives

Other options are cystoscopic stone basket retrieval, lithotripsy, percutaneous cystolithotomy or cystotomy.

Cystoscopic-guided basket retrieval

Indications

This technique **(Box 2)** is suitable for removal of urethral and bladder stones not amenable to medical dissolution and too large to be evacuated by voiding urohydropulsion. Basket retrieval can be considered in female dogs with stones < 5 mm diameter, male dogs with stones < 4 mm (limited by the size of the *os penis*), and female cats with stones < 3-4 mm (8,9). The small diameter of the male cat's urethra prevents cystoscopy with a working channel.

Box 2. At a glance... Cystoscopic basket retrieval.

Size and number of uroliths	Stones < 5 mm in small female dogs
	Stones < 3-4 mm female cats
	Male dogs limited by size of penile urethra (2-3 mm)
Sex and species	Female dogs and cats
	Male dogs > 7 kg (penile urethra must allow passage of the flexible scope)
Advantages	Quick
	No suture material in the bladder
Disadvantages	Specialized equipment

Equipment

This requires a rigid or flexible cystoscope, and a stone basket that can be passed through the working channel of the cystoscope.

Procedure

The patient is anesthetized and placed in dorsal (female) or lateral (male) recumbency. An epidural anesthetic may enhance lower urinary tract relaxation and facilitate stone retrieval. Cystoscopy is used to visualize the urolith(s) and a stone basket is passed through the working channel of the scope to grasp the stone. Under continuous saline flush, the basket is pulled towards the tip of the scope and both scope and basket are then withdrawn. If resistance is felt, the flush pressure can be increased in order to help dilate the urethral lumen and the basket can be gently rotated. If resistance is still felt, the basket should be opened to release the stone and another technique used in order to avoid damage to or perforation of the urethra **(Figure 3)**.

Special considerations

In the presence of urethral stricture/inflammation, the clinician should be prepared to remove the stone using another technique.

Complications

Urethral stricture or perforation is possible during retrieval of embedded or sharp-edged stones.

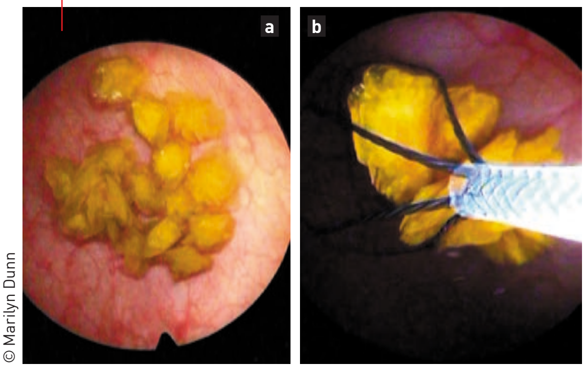
Alternatives

Lithotripsy, percutaneous cystolithotomy or cystotomy may be considered.

"Before deciding on the preferred method for stone removal, radiography should be used to measure the size of the uroliths; ultrasound tends to overestimate urolith size and underestimate the number of uroliths."

Marilyn Dunn

Figure 3. Cytoscopic stone basket retrieval by retrograde cystoscopy. Multiple irregular stones are seen in the bladder **(a)**. A stone basket passed through the working channel of the cystoscope grasps a stone which is then withdrawn, along with the cystoscope, out of the bladder, through the urethra and removed **(b)**.



© Marilyn Dunn

Box 3. At a glance... Intracorporal lithotripsy.

Size and number of uroliths	Low stone burden preferable
Sex and species	Female cats and dogs
	Male dogs > 7 kg
Advantages	No suture material in the bladder
Disadvantages	Specialized equipment
	Long procedural length with large stone burden

Intracorporal lithotripsy

Indications

This technique **(Box 3)** may be used for removal of urethral and bladder stones not amenable to medical dissolution and that are too large to be removed by cystoscopic-guided basket retrieval (10-13).

Equipment

A Hol:Yttrium Aluminium Garnet (Ho:YAG) low power surgical laser with a laser fiber that can be passed through the scope channel, or an electrohydraulic lithotripter; a rigid or flexible cystoscope, and (optionally) a stone basket.

Procedure

The patient is anesthetized and placed in dorsal (female) or lateral (male) recumbency. Cystoscopy is used to visualize the stone. If an electrohydraulic lithotripsy is used, the tip of the fiber is placed in direct contact with the surface of the urolith at an angle of 90°. The stone is fragmented by the lithotriptor's energy transmitted directly to the stone, creating a shock wave that induces fragmentation.

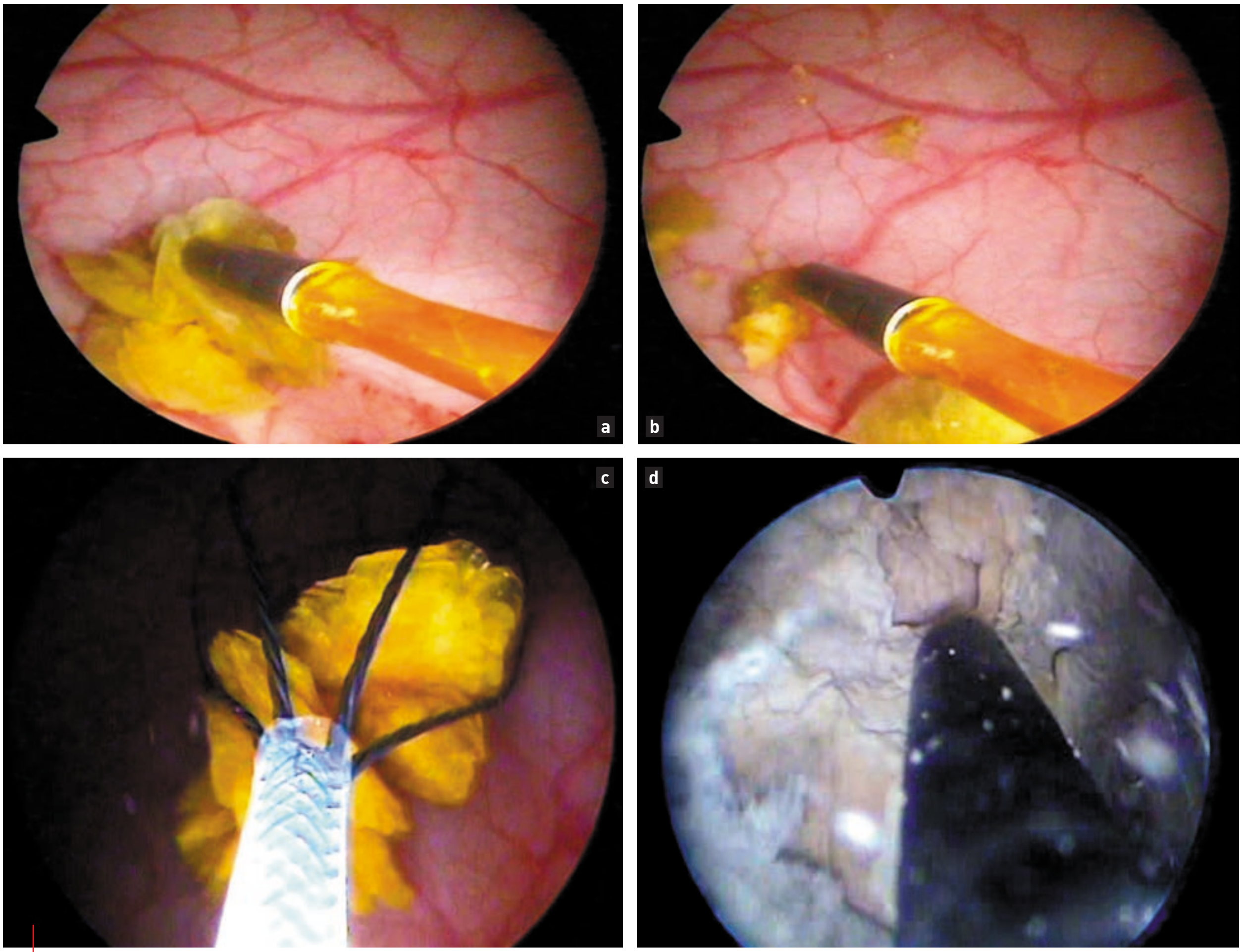


Figure 4. A large stone identified via retrograde cystoscopy in the bladder. A lithotripter probe is advanced through the working channel of the scope until its tip contacts the stone **(a)**. The electrohydraulic lithotripter is activated, resulting in fragmentation of the stone **(b)**. Smaller fragments can be removed by voiding urohydropulsion or a stone basket **(c)**. A lithotripter probe used to fragment a large calcium carbonate stone in a tortoise; note the crater created in the stone by the probe **(d)**.

With the Ho:YAG laser, pulsed laser energy is transmitted from the energized crystal to the urolith via the fiber. The stone is fragmented by a thermal drilling process, in which the pulse energy traveling through the fiber creates a microscopic vapor bubble on the surface of the calculus. This microscopic "parting" of the fluid medium by an air bubble (known as the *Moses effect*) allows the laser's energy to be transmitted directly into the stone, creating a shock wave that induces stone fragmentation.

If the fiber tip is 1 mm or more away from the stone, the vapor bubble collapses, the water or saline absorbs the energy, and no energy is transmitted to the urolith. As the fiber tip is advanced to within 0.5 mm of the calculus, the vapor bubble comes in contact with the stone. The closer the fiber tip is to the target, the larger the effect, with the greatest effect achieved when the fiber is in direct contact with the stone. The energy is absorbed in < 0.5 mm of fluid, making it safe to fragment uroliths in tight locations, such as within the urethra, ureter, renal pelvis, or urinary bladder, with limited risk of adjacent urothelial damage (14).

Stones are fragmented until the pieces are small enough to be voided using urohydropulsion or removed with a stone retrieval basket **(Figure 4)**. One study reported the use of a basket to move smaller bladder stones into the urethra before fragmentation to minimize their movement during lithotripsy, with the technique resulting in more complete fragment removal (11).

Special considerations

The major challenge with this method is removal of stone fragments from the urinary tract, especially in male dogs. Its success depends on careful patient selection. A large number of large stones in a small patient are best removed by PCCL.

Outcome

The Ho:YAG laser is effective on all stone types (14). Complete urolith removal is achieved in 100% of dogs with urethroliths, 83-96% of female dogs with cystoliths, and 68-81% of male dogs with cystoliths (10-13).

Box 4. At a glance... Percutaneous cystolithotomy (PCCL).

Size and number of uroliths	No restrictions
Sex and species	No restrictions
Advantages	Excellent visualization of the entire lower urinary tract and easy retrograde stone removal
Disadvantages	Specialized equipment
	Access to lithotripsy may be necessary for large or embedded stones

Complications

Urethral edema, which is self-limiting, and mild hematuria may be seen. Bladder perforation by the laser is a rare occurrence, and can be treated by leaving a urinary catheter in place for 24-48 hours (10-13).

Alternatives

Percutaneous cystolithotomy, surgical cystotomy and/or urethrotomy.

Percutaneous cystolithotomy (PCCL)

Indications

PCCL **(Box 4)** can be used for removal of urethral and bladder stones that are not amenable to medical dissolution and are too large or too numerous to be removed by voiding urohydropulsion, cystoscopic-guided basket retrieval or lithotripsy. The approach, which is through the bladder apex, can also be used to gain access to the urethra, bladder and ureters (16).

Equipment

A urinary catheter, standard surgical instruments, laparoscopic threaded cannula (trochar) with diaphragm, rigid and flexible cystoscopes, stone basket, lithotripsy (required for embedded stones).

Procedure

The patient is anesthetized and placed in dorsal recumbency. A urinary catheter is placed and sterile saline infused until the bladder apex is palpable. A 1-2 cm ventral midline skin incision is made over the area of the bladder apex into the abdominal cavity. The bladder apex is identified and tissue forceps are used to grasp the apex. Stay sutures are placed and a stab incision is made at

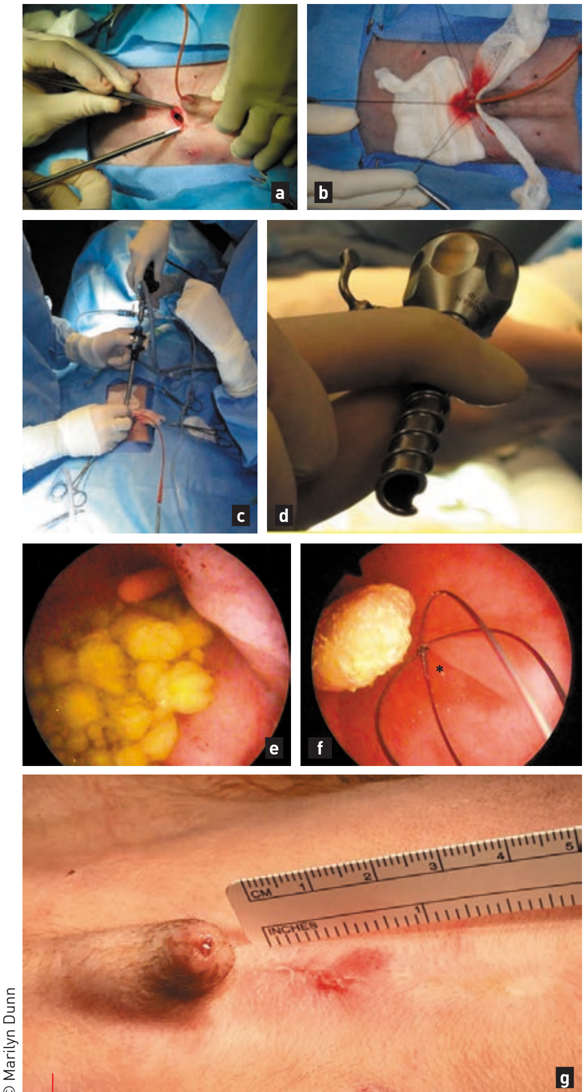


Figure 5. Percutaneous cystolithotomy in a male dog. A 1.5 cm incision is made over the bladder apex **(a)**. The bladder is identified and stay sutures are placed **(b)**. A trocar is placed into the apex of the bladder, and a rigid cystoscope is inserted through the trocar under continuous saline flush **(c)**. The trochar used to enable cystoscopy of the bladder **(d)**. Multiple spiculated stones are visible in the bladder trigone through the trochar; the tip of the orange urethral catheter is also visible **(e)**. A stone basket retrieval device is passed through the working channel of the cystoscope, allowing stone retrieval from the bladder through the trocar. The ureteral papilla is marked with an asterisk **(f)**. A small skin incision remains following the procedure **(g)**.

the bladder apex. The laparoscopic cannula is screwed in place and directed toward the urethral lumen. A rigid cystoscope is advanced through the cannula into the bladder and the stones are identified and removed with the stone basket. Once all bladder stones are removed, the urethra is examined (using a flexible scope in male dogs and a rigid scope in female dogs and cats). Stones in the urethra can be removed with a stone basket or flushed into the bladder and removed. The cannula is withdrawn and the bladder incision and abdomen closed **(Figure 5)** (16).

Outcome

Complete stone removal is achieved in 96% of patients (16).

Complications

Wound infection, dehiscence and uroabdomen are rare potential complications associated with the transabdominal approach.

Other considerations

Stone recurrence is a concern. Laser lithotripsy is occasionally required as larger cystoliths may otherwise need to be removed by stretching/extending the bladder incision. This procedure can be performed on an outpatient basis, but if a patient has a urinary tract infection, antibiotic therapy should be administered prior to the procedure due to the increased risk of septic peritonitis.

Alternatives

Surgical cystotomy and or urethrotomy may be considered.

CONCLUSION

Minimally invasive stone removal is the new standard of care in small animal veterinary medicine. In comparison with standard surgical procedures, the techniques are associated with minimal tissue injury, shorter hospitalizations, smoother recovery and decreased peri-operative morbidity and mortality. A thorough understanding of the therapeutic options available is essential to properly educate and inform the client. Proper equipment, technical expertise and experience are essential prerequisites to many of these procedures. Once stones have been removed and analyzed, developing a proper prevention regime is essential to minimize stone recurrence.

REFERENCES

1. Grant DC, Harper TA, Werre SR. Frequency of incomplete urolith removal, complications, and diagnostic imaging following cystotomy for removal of uroliths from the lower urinary tract in dogs: 128 cases (1994-2006). *J Am Vet Med Assoc* 2010;236:763-766.
2. Appel SL, Lefebvre SL, Houston DM, *et al*. Evaluation of risk factors associated with suture-nidus cystoliths in dogs and cats: 176 cases (1999-2006). *J Am Vet Med Assoc* 2008;233:1889-1895.
3. Thieman-Mankin KM, Ellison GW, Jeyapaul CJ, *et al*. Comparison of short-term complication rates between dogs and cats undergoing appositional single-layer or inverting double-layer cystotomy closure: 144 cases (1993-2010). *J Am Vet Med Assoc* 2012;240:65-68.
4. Urena R, Mendez-Torres F, Thomas R. Complications of urinary stone surgery. In: Stoller ML, Meng MV (eds.) *Urinary Stone Disease: The Practical Guide to Medical and Surgical Management*. Totowa, NJ: Humana Press Inc; 2007:511-553.
5. Carlin BI, Paik M, Bodner DR, *et al*. Complications of urologic surgery prevention and management. In: Taneja SS, Smith RB, Ehrlich RM (eds.) *Complications of Urologic Surgery*. 3rd ed. Philadelphia, PA: WB Saunders; 2001:333-341.
6. Lulich JP, Berent AC, Adams JL, *et al*. ACVIM Small Animal Consensus Recommendations on the Treatment and Prevention of Uroliths in Dogs and Cats. *J Vet Intern Med* 2016;30;1564-1574.
7. Lulich JP, Osborne CA, Carlson M. Nonsurgical removal of uroliths in dogs and cats by voiding urohydropropulsion. *J Am Vet Med Assoc* 1993;203;660-663.
8. Defarges A, Dunn M, Berent A. New alternatives for minimally invasive removal of uroliths: lower urinary tract uroliths. *Comp Cont Educ Small Anim Vet* 2013; 35(1):E1-7.
9. Berent A. New techniques on the horizon: Interventional radiology and interventional endoscopy of the urinary tract ("endourology"). *J Feline Med Surg* 2014;16(1):51-65.
10. Defarges A, Dunn M. Use of electrohydraulic lithotripsy to treat bladder and urethral calculi in 28 dogs. *J Vet Intern Med* 2008;22:1267-1273.
11. Adams LG, Berent AC, Moore GE, *et al*. Use of laser lithotripsy for fragmentation of uroliths in dogs: 73 cases (2005-2006). *J Am Vet Med Assoc* 2008;232:1680-1687.
12. Grant DC, Werre SR, Gevedon ML. Holmium:YAG laser lithotripsy for urolithiasis in dogs. *J Vet Intern Med* 2008;22:534-539.
13. Lulich JP, Osborne CA, Albasan H, *et al*. Efficacy and safety of laser lithotripsy in fragmentation of urocystoliths and urethroliths for removal in dogs. *J Am Vet Med Assoc* 2009;234(10):1279-1285.
14. Lulich JP, Adams LG, Grant D, *et al*. Changing paradigms in the treatment of uroliths by lithotripsy. *Vet Clin North Am Small Anim Pract* 2009;39:143-160.
15. Wynn VM, Davidson EB, Higbee RG, *et al*. *In vitro* effects of pulsed holmium laser energy on canine uroliths and porcine cadaveric urethra. *Lasers Surg Med* 2003;33:243-246.
16. Runge JJ, Berent AC, Mayhew PD, *et al*. Transvesicular percutaneous cystolithotomy for the retrieval of cystic and urethral calculi in dogs and cats: 27 cases (2006-2008). *J Am Vet Med Assoc* 2011;239(3):344-349.

HOW I APPROACH... CANINE URINARY INCONTINENCE

Urinary incontinence is a common presentation to the small animal clinician; Rafael Nickel shares his thoughts on how to approach such cases and discusses some of the newer techniques available for treatment.

KEY POINTS

1. Successful diagnosis of urinary incontinence starts with careful questioning of the owner, followed by urinalysis and ultrasound scans of the patient.
2. Urethral sphincter mechanism incompetence (USMI) is the most common cause of urinary incontinence, and can usually be successfully treated with long-term medication.
3. Ectopic ureter, the most common cause of urinary incontinence in juvenile dogs, is often associated with USMI, which means that surgical correction alone is only successful in some cases.
4. Bladder malfunction and injury leading to urinary incontinence are rarely amenable to successful medical therapy but in selected cases a suprapubic permanent catheter can offer a good quality of life.

Introduction

Urinary incontinence is generally considered as a symptom, presenting as a passive, unconscious dribble of urine from the urogenital tract. There should be no discernible behavioral patterns typical of urination, and a micturition reflex is usually absent. Identification of true incontinence should narrow down the possible causes and pathophysiology, and assist in the diagnosis and assessment of potential treatments, thus allowing a standardized approach to the problem.

How do I proceed?

I tend to start with specific questions to the owner to help with classification and definition, *e.g.*:

- Is it really a passive urine loss?
- Does it occur repeatedly, only at rest or when sleeping, daily or only occasionally, or immediately after a walk? A scoring system is helpful here.
- Did it first occur at a young age or only after sexual maturity?
- Did it occur after neutering, deslorelin implant or similar?
- Are there any issues with conscious urination?
- Is there anything strange about the dog's drinking behavior, *e.g.*, is it polyuric/polydipsic (PU/PD)?
- Is the urine light in color (especially if the dog is PU/PD), or does it have a strong smell (which can indicate urinary retention or infection)?
- Are there signs of neurological deficits (*e.g.*, locomotor disorder or weakness, impaired defecation, etc.)?

Diagnostic investigations

With the information collected, I can plan a more targeted approach and make the list of differential diagnoses more manageable. This can be rather long, as shown in **Table 1**, but in order to identify the majority of possible causes quickly, easily and cheaply, in the interests of the pet and the owner, I recommend performing a minimum database, as follows:

Urine test

A comprehensive analysis and bacteriological examination of urine from a cystocentesis sample is ideal. If the urine specific gravity (USG) is < 1.020, further tests for all causes that can lead to PU/PD should be carried out. Remember that healthy dogs will have a natural daily variation in the USG, and repeated urine samples should be taken as necessary. Although rarely the cause of

Rafael Nickel,

Dr.med.vet., PhD, Dipl. ECVS, Evidensia Tierärztliche Klinik für Kleintiere, Norderstedt, Germany

Professor Nickel qualified from Hannover Veterinary School in 1983 and his career has spanned research, small animal practice and academia. He joined Utrecht University in 1989, where he worked as a specialist and lecturer in surgery and urology – and completed his PhD on canine urinary incontinence – before becoming a partner and manager at a private small animal clinic near Hamburg. As well as holding the ECVS Diploma in small animal surgery, he has Dutch recognition as a small animal surgery specialist and is a visiting lecturer at both the Free University of Berlin and Justus-Liebig University in Giessen.

Table 1. A survey of 563 dogs diagnosed with urinary incontinence at Bristol University *.

Diagnosis	Juvenile dogs		Adult dogs		Total
	female	male	female	male	
Sphincter deficiency (USMI)	64	12	235	9	**320**
Ectopic ureter (EU)	90	10	12	4	**116**
No diagnosis	6	5	12	10	**33**
USMI + EU	15	0	2	0	**17**
Prostate disease	0	0	0	12	**12**
USMI + detrusor instability	8	1	3	0	**12**
Detrusor instability (DI)**	2	0	4	5	**11**
Neoplasia of the bladder	0	0	5	5	**10**
Neurological cause	0	0	3	6	**9**
Cystitis	2	0	5	1	**8**
Pseudo-/ Hermaphroditismus	5	1	1	0	**7**
Fistula (ureterovaginal/ vesicovaginal)	0	0	4	0	**4**
Vaginal neoplasia	0	0	2	0	**2**
Pelvic abscess	0	0	1	0	**1**
Perineal rupture	0	0	0	1	**1**
TOTALS	**192**	**29**	**289**	**53**	**563**

* Holt PE. Urinary incontinence in dogs and cats. Vet Rec 1990;127:347-350.
** Suspected diagnosis or as a result of cystometry investigations

incontinence, any urinary infection is significant, as it can increase the severity of the clinical signs and may adversely affect the response to treatment for the incontinence.

Ultrasound examination

Ultrasound is non-invasive, relatively cheap and commonly available. It is possible to detect structural changes to the kidneys, the course of the ureters, the size, position and contents of the bladder, and the prostate, as well as the emptying function. It is therefore useful to examine the patient with a full bladder and then again after urination. If possible, spontaneous urination should also be observed.

Ultrasound allows assessment of the amount of urine remaining in the bladder after micturition, the so-called *residual urine volume*. Measurement of the bladder in 3 planes (longitudinal, transversal and sagittal), multiplied by a correction factor of 0.625 and then divided by bodyweight allows for precise volume determination***. Residual amounts of urine > 4 mL/kg body weight have been shown to be associated with neurological or obstructive disease (1).

Ultrasound also allows determination of the bladder position within the abdomen. A caudally located bladder, often pear-shaped, or with an abnormal angle between the bladder neck and the proximal urethra, is a common finding in bitches with urethral sphincter mechanism incompetence (USMI). 80-87% of bitches with proven urinary dysfunction present with this condition (2). Ultrasound imaging can identify the degree of hypermobility of the bladder and urethra (3) **(Figure 1)**.

The most common cause of incontinence in juvenile dogs is an ectopic ureter, and this can be identified sonographically in the vast majority of cases (4). Noticeable ultrasonic findings may include a ureter which follows an intramural course in the bladder wall **(Figure 2)**, a dilated ureter and renal pelvis, and a divergent or absent "jet phenomenon".

The "jet phenomenon" describes the normal entrance of urine into the bladder from the ureters, and can often be detected on ultrasound scan.

*** Lisciandro GR, Fosgate GT. Use of AFAST Cysto-Colic View urinary bladder measurements to estimate urinary bladder volume in dogs and cats. *J Vet Emerg Crit Care* 2017;27(6):713-717.

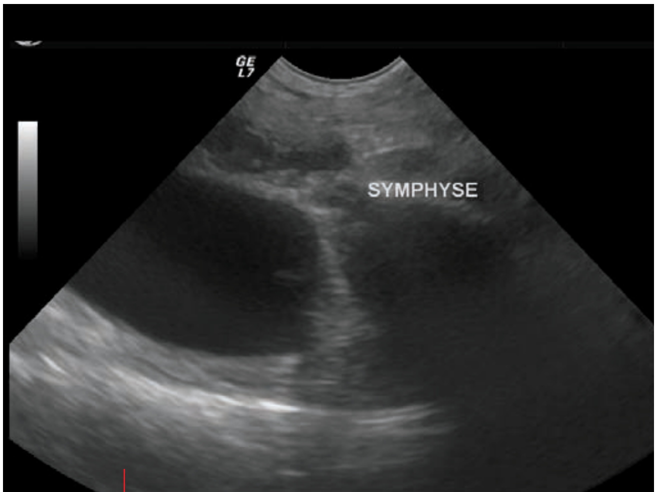


Figure 1. A longitudinal sonographic scan of the caudal abdomen with the hypoechogenic contents of the urinary bladder visible. The typical trough-like shape of the bladder neck cannot be identified because the pubic bone interferes with the intrapelvic image, indicating caudal positioning of the bladder or urethral hypermobility.

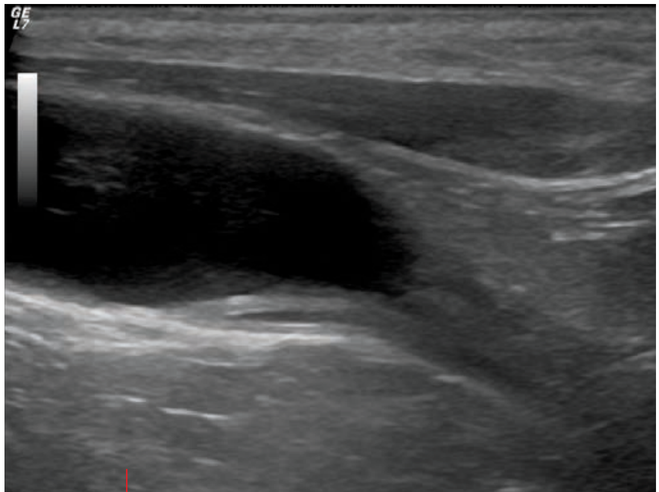


Figure 2. A longitudinal sonographic scan of the caudal abdomen of a dog showing the bladder and bladder neck; the intramural course of an ectopic ureter is clearly visible within the dorsal wall of the bladder neck.

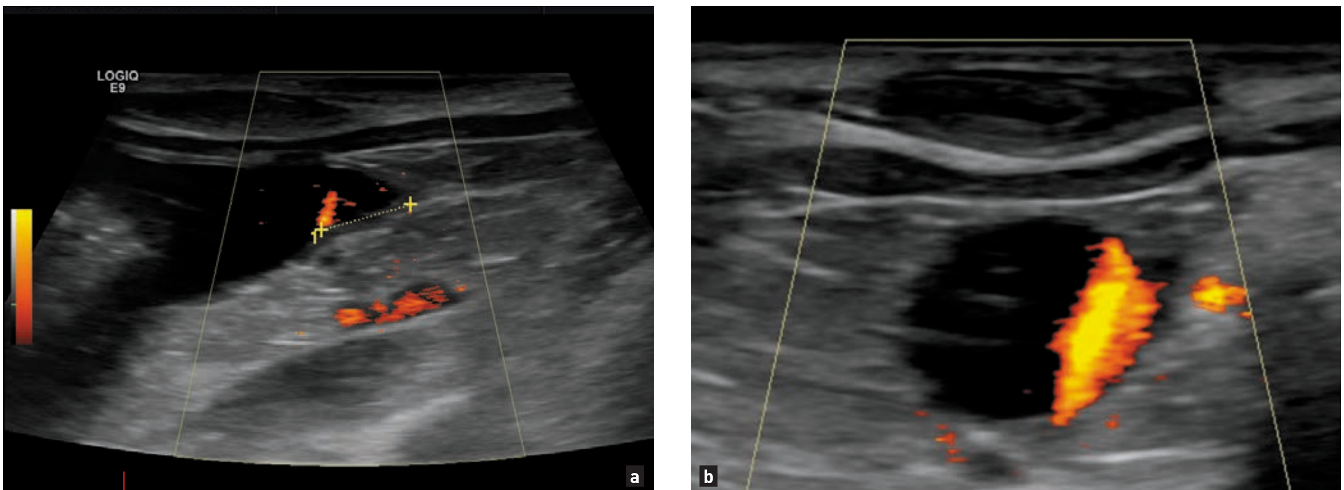


Figure 3. A sonographic scan using color Doppler mode in the area of the bladder neck. A colored jet of urine enters the bladder lumen dorsally through the uretero-vesical junction in a caudal-ventral direction, indicating normal anatomy and function **(a)**. In the transverse scan the normal jets have a "sword-like" appearance **(b)**.

Sufficient ureteric peristalsis from concomitant urine production is necessary, and in puppies and some adult dogs it may be sufficient to offer the patient a drink before performing a scan. Alternatively, furosemide (1-2 mg/kg SC or IV) can be used to stimulate urine production. Following the injection (within a minute if given IV, or approximately 10 minutes if given SC) a longitudinal bladder scan should show a normal jet of urine in a ventrocaudal direction; in a transverse scan, the urine jet is arched, sometimes described as resembling a curved sword **(Figure 3)**.

Not all incontinent patients will have such findings on ultrasound examination, and other possibilities, such as uroliths, tumors, diverticula and unusual abnormalities (*e.g.*, malformations of the urogenital tract, such as pseudohermaphroditism) may be identified.

When do I recommend further investigation?

A definitive diagnosis of urethral sphincter mechanism incompetence (USMI) cannot be confirmed by any method, including computer tomography, magnetic resonance imaging, endoscopy or with urodynamic examination techniques (2). If the history and clinical signs suggest USMI, it may therefore be appropriate to try "diagnostic therapy" as detailed below, using sympathomimetics or hormones (only in neutered dogs), as such drugs will be ineffective if the urinary incontinence is due to other causes. However, a lack of effect does not exclude USMI.

To confirm or rule out an ectopic ureter (EU), computer tomography is recommended (5) although some clinicians report cystourethroscopy is just as effective (6). Personally I only use this latter technique if ultrasound examination gives doubtful results, or if I suspect a combined EU and USMI (7), and to decide which treatment is appropriate.

If endoscopy is unavailable, I would consider retrograde contrast radiography, particularly for cases of juvenile urinary incontinence. Urethrography (in male dogs) and vaginourethrography (in female dogs) **(Figure 4)** can be very helpful for detecting anatomical changes to the urethra. Urodynamic examination methods are only available in a small number of university clinics and are not a routine diagnostic option.

Drug therapy options for USMI

In view of the high success rate and the rare side effects, sympathomimetics and estrogens are almost always my first choice for treating USMI. The drugs work by optimizing the passive resistance of the urethra during the bladder's filling phase, and the efficacy has been assessed using urodynamic examination (8-10).

Phenylpropanolamine and **ephedrine hydrochloride** are sympathomimetics licensed for use in dogs in many European countries. Various retrospective studies have shown phenylpropanolamine to be successful in treating urinary incontinence in 75-97% of cases and ephedrine in 74-93% of cases (11-12). In a comparison with phenylpropanolamine, pseudoephredine, a diastereomer of ephedrine used in the USA and Australia, resulted in more side effects and was less effective (8). Side effects described for sympathomimetics include hypertension, restlessness, anxiety, agitation and tachycardia (8-12). A personal retrospective analysis of patients by Utrecht University between 1990 and 1996 showed such side effects in 24% of cases given ephedrine and in 9% of cases given phenylpropanolamine (unpublished data).

Phenylpropanolamine is dosed at 1-1.5 mg/kg q8-24h PO and ephedrine is dosed at 1-4 mg/kg q8-12h PO. One study noted that while there was no difference between a single dose slow-release formulation and repeated daily use of phenylpropanolamine (12), there was a decrease in the urethral resistance measurements after one week of treatment with the daily dosing protocol (9). A reduction in the receptor sensitivity is suspected with long-term use, but in a personal retrospective analysis, no reduction in effect was observed over a two-year period using phenylpropanolamine at 1.5 mg/kg q12h. Both drugs are less effective in male dogs than in bitches.

Estriol is authorized for the treatment of urinary incontinence in bitches in most European countries, and – in contrast to other estrogens

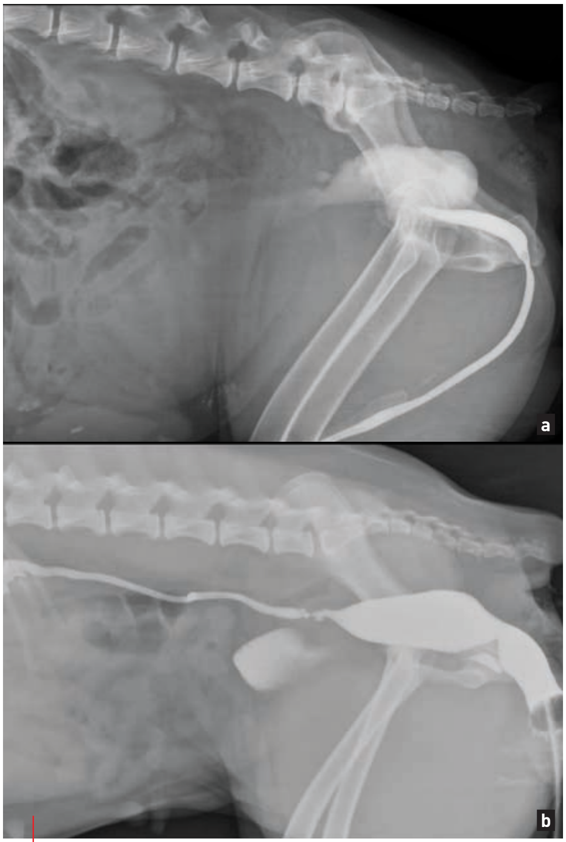


Figure 4. A retrograde contrast radiograph of the lower urinary tract (urethrography) in a male dog with a urethral diverticulum **(a)**. A retrograde contrast radiograph of the vagina, urethra and bladder (vaginourethrography) in a female dog with a ureterovaginal fistula **(b)**.

(*e.g.*, estradiol, diethylstilbestrol, which have a longer receptor binding time) – its use at the recommended dose has not resulted in any bone marrow depression being described to date (13). Note that estriol is only authorized for the treatment of neutered bitches, with a recommended dose of 1 mg per animal q24h PO. However, the effective dose can vary greatly between individual animals, but higher doses may result in unwanted side effects similar to a bitch in heat (*i.e.*, attractiveness to male dogs, vulval swelling and discharge) (14). As demonstrated by urodynamic testing (10,15), the onset of efficacy is longer than that of sympathomimetics; the success rate in one clinical study was 61%, but only after some weeks of use (14).

Estrogen has an effect on the receptor binding of sympathomimetics and can therefore achieve a synergistic effect (16). Personal experience confirms the effect of combination therapy in dogs where sympathomimetics alone are no longer effective, but in one study urodynamic measurements showed that the maximal urethral occlusion pressure decreased after a week on combination therapy when compared to estriol alone (15).

Gonadotropin Releasing Hormone (GnRH) and its analogues, such as buserelin, have been investigated for dogs with USMI (17). One study

> "In view of the high success rate and the fact that side effects are rare, sympathomimetics and estrogens are almost always my first choice for treating urethral sphincter mechanism incompetence."
>
> **Rafael Nickel**

showed that 7 out of 11 bitches were continent when treated with a GnRH analogue (17). However, urodynamic examinations did not show any effect on urethral occlusion pressure and the drug was less effective than phenylpropanolamine. Interestingly, some bitches in the placebo control group also became continent. Anecdotal reports on the use of deslorelin implants (which is licensed in some countries for chemical castration of dogs) suggest it is also effective in some neutered bitches and dogs (18).

Endoscopic and surgical options for USMI

In bitches that do not respond to drug treatment, or where therapy efficacy decreases over time, or there is intolerance to medication, it may be necessary to consider mechanical methods to increase urethral resistance.

For many owners, an attractive option is endoscopic injection of bioimplants into the urethral mucosa **(Figure 5)**. Under general anesthesia three to four deposits of an injectable implant material (collagen or polymer) are inserted in a circular fashion, approximately 1.5 cm distal to the trigone via cystoscopy. The reported success rate is variable, although a long-term study noted 27 out of 40 bitches (68%) showed a good response over an effective period of 1-64 months (an average of 17 months). Side effects, in the form of hematuria and transient stranguria, are generally rare and moderate (19). Various bioimplants have been employed, including collagen; this is no longer available so I have used dextranomer copolymer with hyaluronic acid since 2012. A retrospective analysis of 50 bitches showed no significant difference in progression and effect between the two materials, although numerically the replacement preparation had a lower success rate at 58% (20).

Currently the most popular surgical intervention is implantation of an artificial urethral sphincter (AUS). This is a silicone collar which is inserted around the urethra to partially occlude it (21). The collar is connected to a catheter which leads to a subcutaneous port; this allows the resistance to be adjusted according to the individual needs of the patient by injection of small amounts of sterile saline solution **(Figure 6)**. Again success rates vary, with some bitches being fully continent following the procedure, whilst others show a significant reduction in symptoms. Complications include dysuria, hematuria and urinary tract infection, and success may depend on the compliance of the owners in using the port. In one study of 27 bitches, complications led to the removal of the collar in two animals, but high owner satisfaction was reported with 22 of the animals (21). Personal experience with AUS in more than 40 female and 25 male dogs over a period of more than four years has given similar results and complications. The worst complication is if stenosis or stricture develops at the site of the collar, which requires removal. In these situations, other options such as endoscopic bioimplant injection or (less frequently) techniques such as colposuspension and/or urethropexy or vasopexy may be considered (22,23).

Detrusor instability treatment options

Urinary incontinence may sometimes result from detrusor hyperreflexia, whereby hyperactivity of the detrusor muscle during the bladder's filling phase without an appropriate response from the urethra causes urine leakage. A definitive diagnosis requires the use of simultaneous urethrocystometry (10). In a small number of cases, dogs that do not respond to the drug therapy suggested above for USMI may respond to oxybutynin, a product indicated for use in humans suffering from detrusor instability. In dogs it is effective at a dose of 0.3 mg/kg q8h, although long-term use may cause constipation and reduced tear production.

Ectopic ureter treatment options

Evidence of an ectopic ureter in incontinent animals by imaging or endoscopy does not always mean that surgical correction will lead to continence. This is probably due to the fact that many affected bitches also have USMI (7,24). The success rate for surgical intervention can be increased significantly if the following criteria are identified (7):

- The abnormal ureteral opening is situated caudal to the bladder neck or the proximal urethra.

- The opening of the ureter or the associated renal pelvis is dilated.
- The bladder is in a normal position.

If these criteria are not met, the likelihood of USMI is substantially higher. In such cases, phenylpropanolamine can be used on a trial basis, even in puppies. I therefore recommend drug treatment is continued until sexual maturity before further intervention. If there is an unsatisfactory outcome I will then perform endoscopic laser ablation (see below) and, if necessary, bioimplant injections into the urethral submucosa.

Endoscopic-assisted laser ablation **(Figure 7)** is an attractive technique for treating EU but the results are only satisfactory in male dogs (25). The technique involves transecting the medial wall of the ectopic ureter with a laser so that it opens into the bladder lumen. In bitches, where there is usually a long intramural ureter, the sphincter muscle mechanism may be compromised, which means the success rate is lower than with surgical techniques (26). Extramural ectopic ureters (which are rare) cannot be corrected using this method.

The classic surgical method for treating EU is ureteroneocystostomy, in which the ectopic section of the ureter is ligated or partially removed and the normal ureter portion inserted and sutured within the bladder mucosa (26). The exact implantation site is not significant, but using spatulation and special stitching techniques can largely avoid the

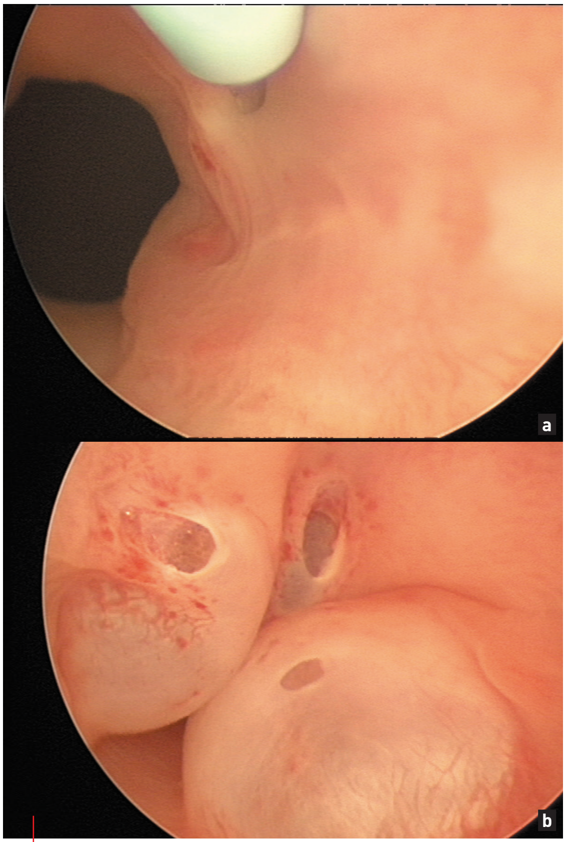


Figure 5. An endoscopic image of the mid-urethral region in a female dog with USMI which had not responded to medical management; a cystoscopic needle (5 Fr) is inserted into the urethral submucosa **(a)**. Three injections of dextranomer co-polymer and hyaluronic acid (each approximately 0.3-0.8 mL) have been placed in the submucosal layer to attain urethral “bulking” **(b)**.

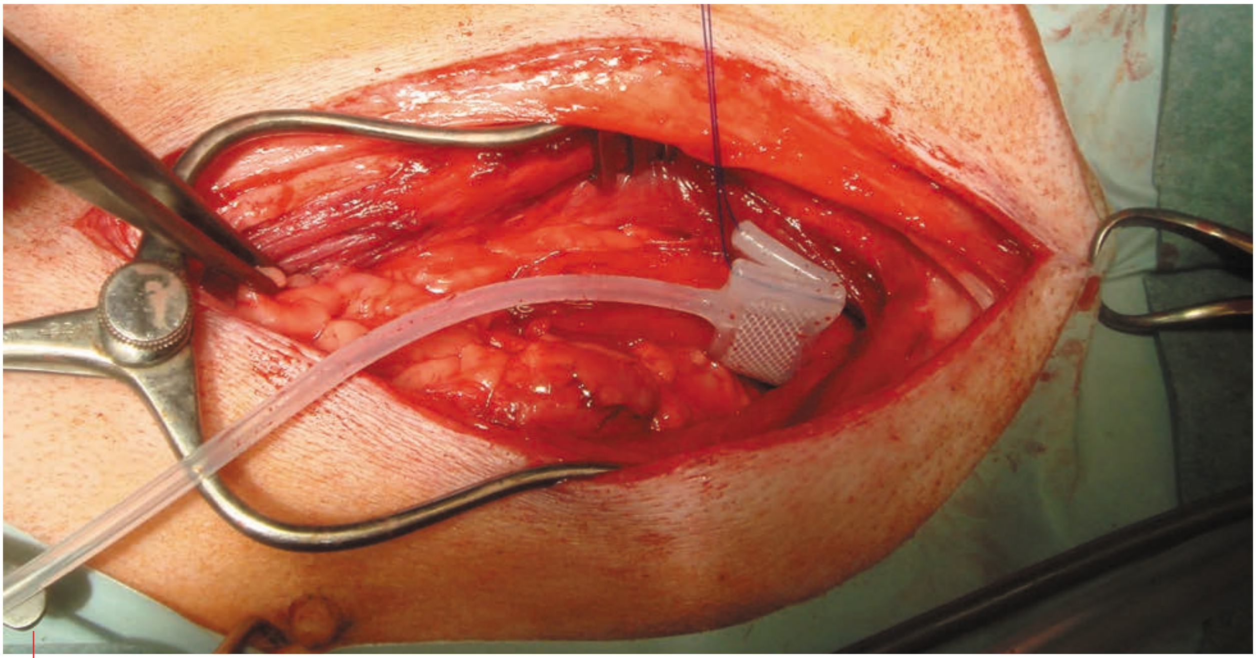
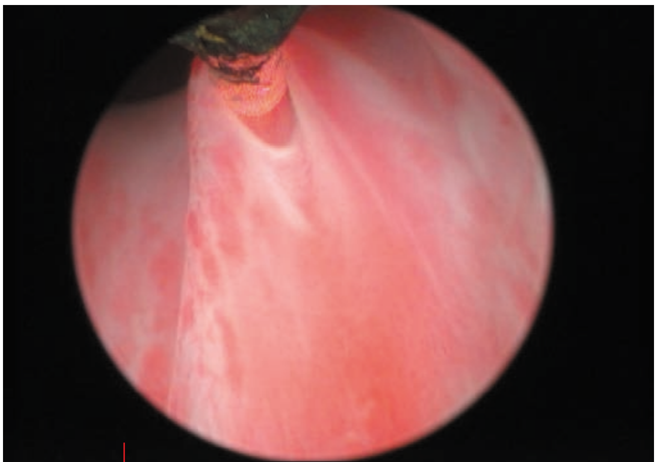


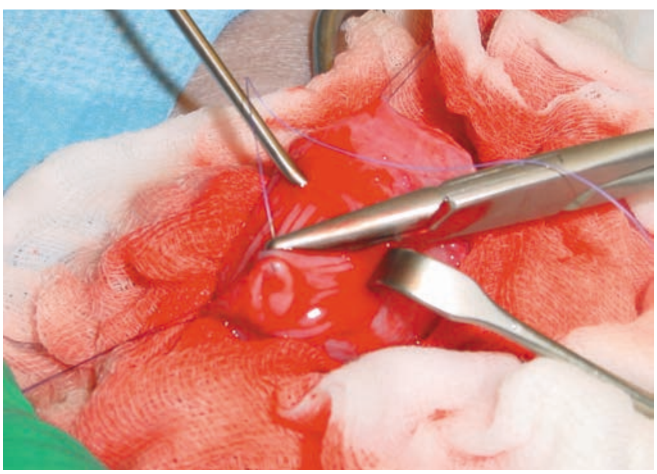
Figure 6. A peri-operative image during surgical placement of an artificial urethral sphincter (AUS) around the cranial urethra. The small silicone tube will be tunneled to connect to a subcutaneous port and saline can be injected via the port to allow subsequent adjustment of the pressure on the urethra.

risk of post-operative stenosis at the anastomosis site **(Figure 8)**. An antegrade catheter inserted to ensure constant urine flow during the first 24 hours post-surgery significantly reduces the risk of complications such as dehiscence and uroabdomen. Using this method, 72% of dogs in one study became continent (26) and my own retrospective study of 20 bitches gave a success rate of 80% (27).



© Rafael Nickel

Figure 7. An endoscopic image showing ectopic ureters entering the cranial urethra. Treatment was via laser ablation.



© Rafael Nickel

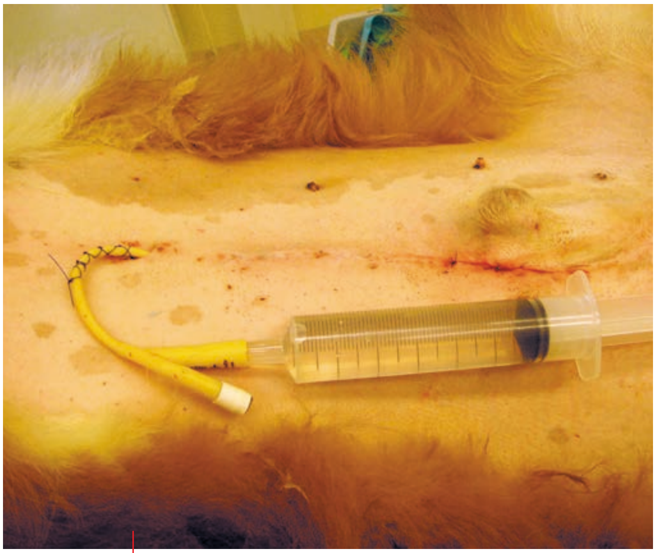
Figure 8. A peri-operative image during surgical correction of an ectopic ureter (ureteroneocystostomy). The abnormal section of the ureter has been ligated and dissected, and the remainder of the ureter is pulled through a stab incision in the bladder wall and anchored to the mucosa with simple interrupted sutures using 4-0 or 6-0 USP monofilament resorbable material.

Bladder dysfunction treatment options

Inadequate emptying of the bladder often leads to urinary incontinence, with the classic form known as overflow incontinence. However, sometimes a dog can appear able to urinate, with partial emptying of the bladder, due to increased intra-abdominal pressure. Some of the underlying causes, such as intervertebral disc disease and spinal cord trauma, are reversible, but prolonged overstretching of the bladder, which can occur with both functional and mechanical obstruction, can result in irreversible damage to the detrusor muscle. Idiopathic paralysis of the bladder is also a possibility.

Regardless of the cause and the prognosis, management of these cases requires the bladder to be emptied at least once a day. In contrast to cats, physical expression is unsuccessful in the majority of dogs, and it is necessary to use either intermittent catheterization or implant a permanent indwelling catheter. Intermittent catheterization can present technical and logistical problems; it may be possible for a pet owner to catheterize a male dog, but it can be much more difficult in small bitches. In addition, long-term intermittent catheters can cause many animals to develop infections which can lead to death or euthanasia (28).

A suprapubic catheter technique has proven to be a relatively uncomplicated method to treat this condition and is generally well accepted by owners. Surgery involves making a very small incision to place a Foley catheter within the bladder, exteriorizing the catheter via a subcutaneous tunnel. Typically I use a catheter 30 cm in length, with about 20 cm retained within the patient. Regardless of the size of the animal, I prefer to site the catheter exit cranial to the umbilicus wherever possible **(Figure 9)**. The long subcutaneous route acts as a barrier to ascending infection and allows a better passive closure. The connective tissue canal formed around the catheter becomes fibrous over time, which assists with the subsequent replacement of the catheter. I routinely recommend this is done after 3 months for aseptic and technical reasons, and if a large diameter catheter (*e.g.*, > 12 Charr./Fr.) is used this makes removal or replacement easier. The balloon at the catheter tip holds the catheter in position within the bladder and is inflated using isotonic saline, usually between 3-15 mL. Management requires careful handling of the tube and drainage of the bladder several times a day. Complications include accidental catheter removal or damage (in ~15% of cases) and infection (in ~20% of patients) (29). Over a 5-year period I have successfully performed 35 such operations, 14 of them for neurological causes and 21 with obstructive neoplasia of the urethra.



© Rafael Nickel

Figure 9. Surgical placement of a Foley catheter in the bladder with a subcutaneous tunnel to the exterior for long-term management of bladder paralysis in a male dog.

CONCLUSION

Canine urinary incontinence is a significant problem which affects the quality of life for both the animal and the owner. It can lead to serious health problems and it is not uncommon for affected dogs to be rehomed or euthanized. Initial ultrasound examination allows many causes to be recognized and treated in a targeted manner, and for the commonest causes of incontinence there are a multitude of treatment options with acceptable success rates and few serious complications.

REFERENCES

1. Atalan G, Barr FJ, Holt PE. Frequency of urination and ultrasonographic estimation of residual urine in normal and dysuric dogs. *Res Vet Sci* 1999;67(3):295-299.
2. Nickel RF, Vink-Noteboom M, van den Brom WE. Clinical and radiographic findings compared with urodynamic findings in neutered female dogs with refractory urinary incontinence. *Vet Rec* 1999;145:11-15.
3. Atalan G, Holt PE, Barr FJ. Ultrasonographic assessment of bladder neck mobility in continent bitches and bitches with urinary incontinence attributable to urethral sphincter mechanism incompetence. *Am J Vet Res* 1998;59(6):673-679.
4. Lamb CR, Gregory SP. Ultrasonographic findings in 14 dogs with ectopic ureter. *Vet Radiol Ultrasound* 1998;39:218-223.
5. Samii VF, McLoughlin MA, Mattoon JS, *et al*. Digital fluoroscopic excretory urography, digital fluoroscopic urethrography, helical computed tomography, and cystoscopy in 24 dogs with suspected ureteral ectopia. *J Vet Intern Med* 2004;18(3):271-281.
6. Cannizzo KL, McLoughlin MA, Mattoon JS. Evaluation of transurethral cystoscopy and excretory urography for diagnosis of ectopic ureters in female dogs: 25 cases (1992-2000). *J Am Vet Med Assoc* 2003;223:475-481.
7. Wiegand U, Nickel R, van den Brom W. Zur Prognose bei der Behandlung von ektopischen Ureteren beim Hund. *Kleintierpraxis* 1996;41:157-16.
8. Byron JK, March PA, Chew DJ, *et al*. Effect of phenylpropanolamine and pseudoephedrine on the urethral pressure profile and continence scores of incontinent female dogs. *J Vet Intern Med* 2007;21(1):47-53.
9. Carofiglio F, Hamaide A, Farnir F, *et al*. Evaluation of the urodynamic and hemodynamic effects of orally administered phenylpropanolamine and ephedrine in female dogs. *Am J Vet Res* 2006;67:723-730.
10. Nickel RF. Studies on the function and dysfunction of the urethra and bladder in continent and incontinent female dogs. *PhD Thesis*, Utrecht University 1998;11-126.
11. Arnold S, Arnold P, Hubler M, *et al*. Incontinentia urinae bei der kastrierten Hündin: Häufigkeit und Rassedisposition. *Schweiz Arch Tierheilk* 1989;131:259-263.
12. Bacon NJ, Oni O, White RAS. Treatment of urethral sphincter mechanism incompetence in 11 bitches with a sustained-release formulation of phenylpropanolamine hydrochloride. *Vet Rec* 2002;151:373-376.
13. Janszen BPM, van Laar PH, Bergman JGHE. Treatment of urinary incontinence in the bitch: a pilot field study with Incurin®. *Vet Q* 1997;19:S42.
14. Mandigers P, Nell T. Treatment of bitches with acquired urinary incontinence with oestriol. *Vet Rec* 2001;22;764-767.
15. Hamaide AJ, Grand JG, Farnir F, *et al*. Urodynamic and morphologic changes in the lower portion of the urogenital tract after administration of estriol alone and in combination with phenylpropanolamine in sexually intact and spayed female dogs. *Am J Vet Res* 2006;67(5):901-908.
16. Creed K. Effect on hormones on urethral sensitivity to phenylephrine in normal and incontinent dogs. *Res Vet Sci* 1983;34;177-181.
17. Reichler IM, Hubler M, Jöchle W, *et al*. The effect of GnRH analogs on urinary incontinence after ablation of the ovaries in dogs. *Theriogenology* 2003;60(7):1207-1216.
18. Lucas X. Clinical use of deslorelin (GnRH agonist) in companion animals: a review. *Reprod Domest Anim* 2014;49 Suppl 4:64-71.
19. Arnold S, Jäger P, Dibartola P, *et al*. Treatment of urinary incontinence in dogs by endoscopic injection of teflon. *J Am Vet Med Assoc* 1989;195:1369-1374.
20. Lüttmann K, Merle R, Nickel R. Retrospective analysis after endoscopic urethral injections of glutaraldehyde-cross-linked-collagen or dextranomer/hyaluronic acid copolymer in bitches with urinary incontinence . *J Small Anim Pract* 2019;60(2):96-101.
21. Reeves L, Adin C, McLoughlin M, *et al*. Outcome after placement of an artificial urethral sphincter in 27 dogs. *Vet Surg* 2013;42(1):12-18.
22. Martinoli S, Nelissen P, White RAS. The outcome of combined urethropexy and colposuspension for management of bitches with urinary incontinence associated with urethral sphincter mechanism incompetence. *Vet Surg* 2014;43(1):52-57.
23. Weber UT, Arnold S, Hubler M, *et al*. Surgical treatment of male dogs with urethral sphincter mechanism incompetence. *Vet Surg* 1997;26:51-56.
24. Holt PE, Moore AH. Canine ureteral ectopia: an analysis of 175 cases and comparison of surgical treatments. *Vet Rec* 1995;136:345-349.
25. Berent AC, Mayhew PD, Porat-Mosenco Y. Use of cystoscopic-guided laser ablation for treatment of intramural ureteral ectopia in male dogs: four cases (2006-2007). *J Am Vet Med Assoc* 2008;232:1026-1034.
26. Reichler IM, Eckrich Specker C, Hubler M, *et al*. Ectopic ureters in dogs: clinical features, surgical techniques and outcome. *Vet Surg* 2012;41(4):515-522.
27. Nickel RF. Ectopic ureters-concurrent urethral sphincter mechanism incompetence: treatment with urethral bulking. In; *Proceedings*, ECVS Annual Scientific Meeting, Barcelona, Spain 2012;148-150.
28. Diaz Espineira MM, Viehoff FW, Nickel RF. Idiopathic detrusor-urethral dyssynergia in dogs: a retrospective analysis of 22 cases. *J Small Anim Pract* 1998; 39:264-270.
29. Beck AL, Grierson JM, Ogden DM, *et al*. Outcome of and complications associated with tube cystostomy in dogs and cats: 76 cases (1995-2006). *J Am Vet Med Assoc* 2007;230:1184-1189.

URINALYSIS: WHAT CAN GO WRONG?

Paola Scarpa,

DVM, PhD, Department of Veterinary Medicine, University of Milan, Lodi, Italy

Professor Scarpa graduated from the Faculty of Veterinary Medicine in Milan and studied for her PhD at the same university. She is currently Associate Professor at Milan with clinical interests that are focused around small animal urology, nephrology and related clinical pathologies.

KEY POINTS

Dipsticks are inexpensive and – assuming correct use – offer a simple qualitative and semi-quantitative test for urinalysis.

1

A urine protein to creatinine ratio may be indicated if a sample is proteinuric, although care must be taken when interpreting the results.

2

Although urinalysis is a routine and everyday test for all small animal practices, there are various potential pitfalls that can markedly affect the reliability of the results obtained, as Paola Scarpa explains.

Introduction

Urinalysis is one of the most common and easiest tests performed in small animal practice, but a surprising number of factors can lead to potential inaccuracies in the results. This short paper identifies some common pitfalls and offers tips on how to achieve best practice for urinalysis.

Urine sample collection

Urine collection must be carried out by an appropriate method. Cystocentesis, preferably guided by ultrasound **(Figure 1)**, is necessary whenever urine culture is required, as it can allow an uncontaminated sample to be obtained. The needle is inserted into the ventral or ventrolateral wall of the bladder at a 45° angle; this allows the muscle fibers of the bladder to rapidly close the hole caused by withdrawal of the needle. The patient must be immobile and calm, usually in lateral or dorsal recumbency, and the sampling area is generally shaved and disinfected prior to inserting the needle. Iatrogenic microhematuria often occurs following the procedure. Cystocentesis is contraindicated if the bladder is empty, if the patient is non-compliant, or if pyoderma is present. Note that metastatic dissemination along the needle has been reported in a case of transitional cell carcinoma of the bladder (1).

Spontaneous urination (Figure 2) is the least traumatic method of collection, although it is not always easy (*e.g.*, in small dogs) or even possible (with cats). Only samples collected in suitable sterile containers should be accepted for analysis. Detergents and disinfectants used to clean containers and litter trays may alter the results of the dipstick test.

Figure 1. Cystocentesis, preferably via ultrasound, allows an uncontaminated urine sample to be obtained.

Figure 2. Spontaneous urination is the least traumatic method of collection, although it is not always easy, and samples must be collected in suitably sterile containers.

Figure 3. Urinary dipsticks are inexpensive and offer a simple qualitative and semi-quantitative test.

A spontaneous urination sample is generally suitable for a "standard" (*i.e.*, first screening) urine test, although note that the sample may be contaminated by prostatic fluid, sperm or debris from the urethra and prepuce. With this caveat, the determination of dipstick proteinuria and UPC ratio is not influenced by the method of collection, so analysis of this type of sample may be satisfactory for diagnosing and monitoring a protein-losing nephropathy. Furthermore, the UPC in cats is not affected by the sampling method (*e.g.*, cystocentesis or by manual compression of the bladder).

Proteinuria

An initial evaluation of proteinuria can be made with a dipstick **(Figure 3)**. The protein pad is impregnated with indicators (*e.g.*, tetrabromophenol blue) that interact with the amine groups of urinary proteins; the resulting color change (from yellow to green and finally to blue) allows a numerical interpretation of the degree of proteinuria, usually assessed from 0-4. This method is sensitive for detection of albumin, but less sensitive for globulins or protein fractions (*e.g.*, Bence-Jones proteins), which typically have lower levels of amine groups.

Various factors, including an alkaline pH, presence of hemoglobinuria, pyuria or bacteriuria, or the use of quaternary ammonium or chlorhexidine disinfectants when collecting samples, can result in false positives.

In dogs, interpretation of the dipstick results along with the urine specific gravity (USG) may indicate when it is necessary to evaluate the UPC ratio **(Table 1)**. Dipstick negative subjects may be considered non-proteinuric, while subjects with a USG < 1.012 and 1+ on the dipstick test should be considered proteinuric. Subjects with 2+ on dipstick are definitely proteinuric.

The UPC ratio

Values above 0.4 in cats and 0.5 in dogs are indicative of renal proteinuria. However, in order to correctly interpret the test result it is important to be aware of the possible biological and analytical variables, as follows:

Daily variability

To have a reliable estimate of proteinuria, it is generally necessary to determine the UPC ratio over several consecutive days and to calculate the mean value. Alternatively, the UPC ratio may be determined from a pooled sample taken over three consecutive days. Since the ratio can vary

Table 1. Assessing the USG and protein dipstick result can help determine if a UPC ratio should be obtained (2).

USG	Protein level = 0	Protein level 1+	Protein level 2+
< 1.012	Non-proteinuric	Likely proteinuric Perform UPC	Proteinuric Perform UPC
> 1.012 – < 1.030	Non-proteinuric	Non-proteinuric	Proteinuric Perform UPC
> 1.030	Non-proteinuric	Non-proteinuric	Proteinuric Perform UPC

Table 2. The mean UPC ratio should be calculated using samples collected over several consecutive days. Since the ratio can vary considerably, two serial samples can only be considered significantly different if the variance is ~80% for low UPC values and ~35% for high UPC values (3).

UPC (baseline)	UPC definitely decreased	UPC definitely increased	Number of samples for reliable quantitation of proteinuria
0.5	< 0.1	> 0.9	1
1	< 0.3	> 1.7	1
2	< 0.9	> 3.1	1
4	< 2.1	> 5.9	1
6	< 3.5	> 8.8	2
8	< 4.9	> 11.1	3
10	< 6.3	> 13.7	4
12	< 7.8	> 16.2	5

considerably over several days, when assessing UPC on an ongoing basis, two serial samples can only be considered significantly different if the variance is ~80% for low UPC values (*i.e.*, around 0.5) and ~35% for high values (*i.e.*, around 12). One measurement is adequate to reliably estimate the UPC when UPC < 4, but 2-5 determinations are necessary at higher UPC values **(Table 2)**.

Analytical variability

The coefficients of variation (CV) of the UPC ratio are 10-20% where the UPC = 0.2 and around 10% for UPC = 0.5. This analytical inaccuracy can then lead to a sub-staging error, especially around the extremes of the "borderline" values, *i.e.*, a patient may be wrongly classified as being non-proteinuric when the UPC value is around 0.15-0.25, or wrongly classified as being proteinuric when the UPC is around 0.45 to 0.55 **(Figure 4)**.

Laboratory method

The UPC ratio may be obtained by different methods (Coomassie Brilliant Blue and Pyrogallol Red) which can lead to differing results (with a mean difference of 0.1-0.2). It is therefore advisable to always refer to the same laboratory to avoid further variation.

Urinary sediment

The presence of contaminants such as blood (macroscopic hematuria) **(Figure 5)** and/or pyuria **(Figure 6)** will lead to a significant increase in the UPC ratio. In cats, this increase is also seen with microhematuria. It may be better to avoid performing a UPC on a sample with an "active" sediment, and if urolithiasis, urinary infection or feline idiopathic cystitis is present it is therefore appropriate to determine the UPC ratio after resolution of the disease.

Gender

Intact male dogs may have a UPC between 0.2 and 0.5, but this can drop to below 0.2 after castration.

Place of collection

The UPC is higher when the urine is collected in a clinical environment rather than in a domestic environment.

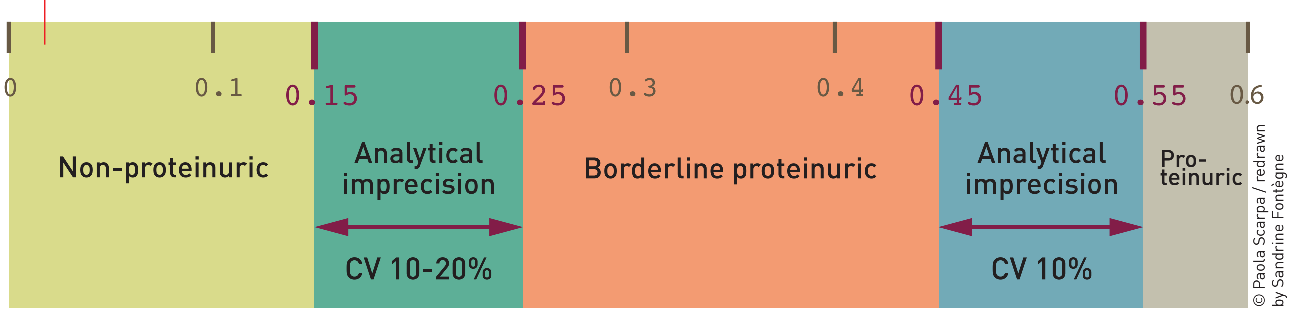
Sample handling and storage

Storing a urine sample before testing can potentially cause several problems.

Bilirubin

It is important to note that bilirubin is an unstable compound, easily oxidizing to biliverdin when exposed to light or air. For this reason, bilirubinuria should be determined within 30 minutes of collection when using a dipstick.

Figure 4. Imprecision in the analysis of the UPC ratio can lead to erroneous interpretation of the result. The coefficients of variation of the UPC ratio are approximately 10-20% where the UPC = 0.2 and around 10% when the UPC = 0.5 (4).



> "An initial evaluation of proteinuria can be made with a dipstick, but while this method is sensitive for detection of albumin, it is less sensitive for globulins or protein fractions."
>
> **Paola Scarpa**

Ketones

The dipstick test for ketones can give a false negative result if the sample to be analyzed has been exposed to air for more than 2 hours, if the pad has been exposed to light, heat or humidity, or if the urine is very acidic.

Temperature

Refrigeration preserves many of the chemical and physical characteristics of urine, but the sample must be brought back to room temperature before performing a dipstick analysis to avoid analytical errors such as inhibition of the glucose reaction. Refrigeration also inhibits bacterial overgrowth, but causes precipitation of calcium oxalate and struvite crystals; these will increase in number and size with time **(Figure 7)**. When performing a UPC ratio, the sample is stable at both room temperature and at +4°C for up to 12 hours post-sampling; after this timepoint the UPC ratio will tend to increase, so it is advisable to freeze the supernatant to reduce any artifacts from long-term conservation.

Technique

The dipstick container must be kept tightly sealed at all times and the expiration date of the test strips verified. Accurate interpretation of dipstick results depends on reading the color change at the specified time for each parameter, and a timer can be used if necessary. Very dark or concentrated urine can also change the dipstick color response, and tests should be repeated as necessary to ensure accurate results.

CONCLUSION

Whilst urinalysis is a commonplace, invaluable and simple diagnostic tool, errors in sample collection, storage and testing parameters may lead to inaccurate outcomes; in addition, correct interpretation of certain results, especially the UPC ratio, can be problematic. The clinician should bear these factors in mind whenever urine tests are required.

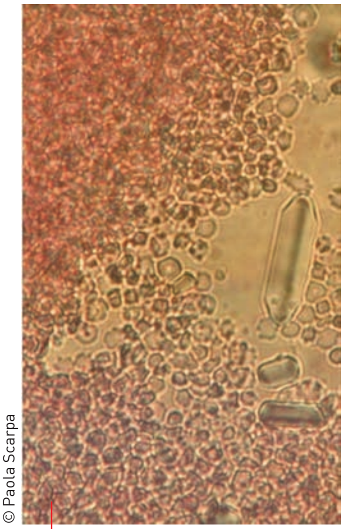


Figure 5. The presence of blood contamination (macroscopic hematuria) in a urinary sediment leads to a significant increase in the UPC ratio.

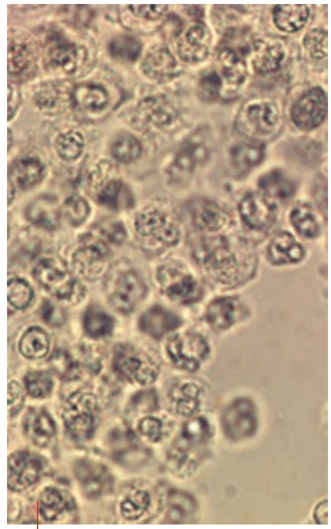


Figure 6. Pyuria in a urinary sediment will also significantly increase the UPC ratio.

Figure 7. Refrigeration of a urine sample can cause precipitation of struvite crystals.

REFERENCES

1. Vignoli M, Rossi F, Chierici C, *et al*. Needle tract implantation after fine needle aspiration biopsy (FNAB) of transitional cell carcinoma of the urinary bladder and adenocarcinoma of the lung. *Schweizer Archiv für Tierheilkunde* 2007;149;314-318.
2. Zatelli A, Paltrinieri S, Nizi F, *et al*. Evaluation of a urine dipstick test for confirmation or exclusion of proteinuria in dogs. *Am J Vet Res* 2010;236(4):439.
3. Nabity MB, Boggess MM, Kashtan CE, *et al*. Day-to-day variation of the urine protein: creatinine ratio in female dogs with stable glomerular proteinuria caused by X-linked hereditary nephropathy. *J Vet Intern Med* 2007;21(3):425-430.
4. Rossi G, Giori L, Campagnola S, Zatelli A, *et al*. Evaluation of factors that affect analytic variability of urine protein-to-creatinine ratio determination in dogs. *Am J Vet Res* 2012;73:779-788.

FRONT LINE ULTRASOUND IMAGING OF THE FELINE URINARY TRACT

Most practices will have access to an ultrasound machine; in this paper Greg Lisciandro discusses how a structured approach to abdominal scanning can help rapid identification of potential bladder abnormalities and related problems.

KEY POINTS

1. Point-of-care ultrasound is gaining more and more use in first opinion veterinary medicine, and can be regarded as the clinician's first-choice imaging method.

2. A structured approach to abdominal scanning should minimize the risk of missing important pathologies.

3. Assessment of bladder volume using ultrasound offers an indirect, non-invasive method for estimation of urine output, which can be important in managing critical cases.

4. Recording ultrasound findings using specific templates helps to emphasize the objectives whilst imaging, as well as chronicling patient data for future reference and comparison.

Introduction

The well-defined point-of-care method for rapid ultrasound scanning of small animals, known as Global FAST or GFAST (Focused Assessment with Sonography in Trauma/Triage) is now widely used in the veterinary community. The technique includes protocols for abdominal scanning (AFAST), thoracic scanning (TFAST), and lung assessment (Vet BLUE, or veterinary Bedside Lung Ultrasound Examination). The idea behind GFAST was to develop a method for standardized ultrasound examination specifically tailored for veterinary patients that would answer clinical questions that might differ from what complete abdominal ultrasound and comprehensive echocardiography were trying to achieve. It should be emphasized that the AFAST, TFAST and Vet BLUE examinations are not the same as "flashing" the abdomen, thorax, and lungs.

The GFAST technique uses defined acoustic windows (*i.e.*, views), which include target-organ interrogation and specific, standardized probe maneuvers. This article focuses on assessment of the feline urinary bladder and considers potential findings using the AFAST Cysto-Colic View (CC), including identification of free fluid and obvious, easily detected bladder abnormalities. The recording of findings on goal-directed templates gives value to the objective examination.

Firstly, however, a word of caution, the veterinary point-of-care ultrasound (V-POCUS) movement lends itself to "satisfaction of search error" through selective imaging (picking and choosing). Without following a standardized global protocol, the clinician will miss pathology and fail to integrate other important ultrasound findings (1-5). The idea is that the GFAST ultrasound approach serves as an extension of the physical exam, as it is designed as a standardized, achievable format for the non-specialist radiologist veterinarian, and is intended to be the clinician's first-line choice of imaging modality, *i.e.*, it is a quick assessment test.

This paper offers an introduction to first-line use of GFAST to assess feline lower urinary tract disease. The AFAST technique is used for general assessment of the abdomen, including a free-fluid scoring system, and is a target-organ approach involving the urinary bladder. A subsequent paper will focus on using the approach to assess patients with kidney disease. TFAST and Vet BLUE methods should also be employed when staging feline patients and for overall volume status. The GFAST approach should be part of the work-up for all cats with urinary tract signs and those with urinary obstruction, but using it as a first-line imaging test may also detect incidental and unexpected findings within the urinary tract.

Gregory Lisciandro,

DVM, Dipl. ACVECC, Dipl. ABVP, Hill Country Veterinary Specialists, Spicewood, Texas

Dr. Lisciandro qualified from Cornell University, completed a rotating internship in small animal medicine and surgery at The Animal Medical Center, New York City, and a residency in Emergency and Critical Care in Texas. He has spent approximately half of his career in general practice and half in emergency and critical care, and his main interest is in point-of-care ultrasound. He has published many clinical studies and is currently co-owner of a specialist small animal practice and CEO of FASTVet.com, an education-based veterinary ultrasound company.

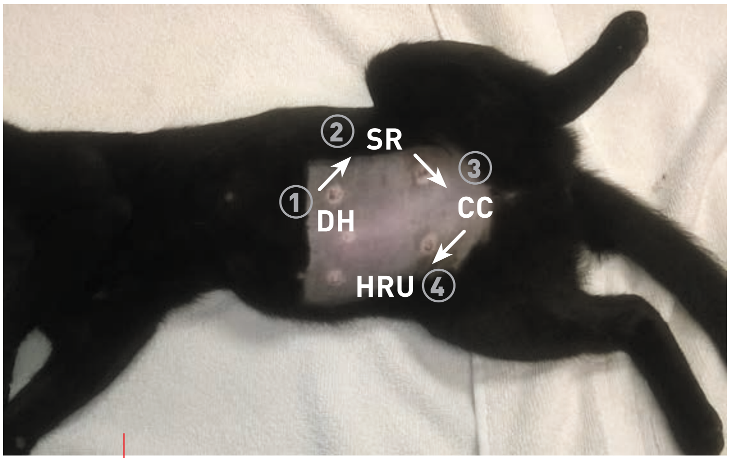


Figure 1. AFAST landmarks on a cat in right lateral recumbency. The cat is sedated in preparation for an elective ovariohysterectomy; for the ultrasound scan the cat would generally not be sedated and not shaved, but the shaved abdomen helps better show the anatomical landmarks.

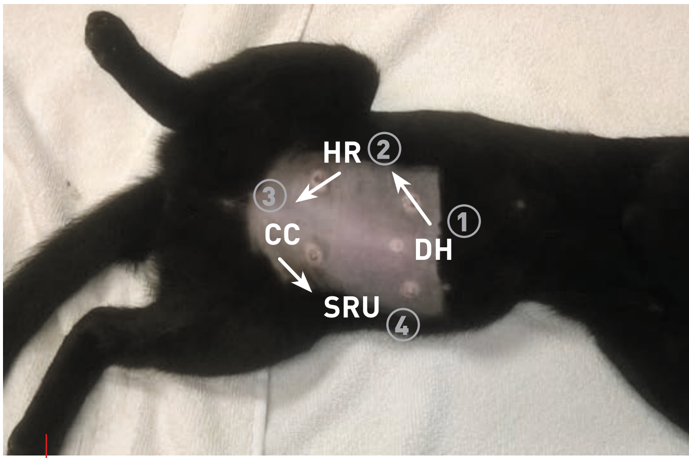


Figure 2. AFAST landmarks on a cat in left lateral recumbency.

DH = Diaphragmatico-Hepatic View; SR = Spleno-Renal View; CC = Cysto-Colic View; HRU = Hepato-Renal Umbilical View; HR = Hepato-Renal View; SRU = Spleno-Renal Umbilical View

The AFAST examination

The external landmarks for the respective AFAST views that are part of the abdominal fluid scoring system are shown in **Figures 1 and 2**. The standardized approach is necessary, beginning with the Diaphragmatico-Hepatic View (DH), followed by the least gravity-dependent Spleno-Renal View (SR) in right lateral recumbency (or the Hepato-Renal View (HR) in left lateral recumbency) followed by the Cysto-Colic View (CC) and then ending at the most gravity dependent Hepato-Renal Umbilical View (HRU) (or the Spleno-Renal Umbilical View (SRU) in left lateral recumbency). The standardized order ensures that the patient's thorax is first screened (*i.e.*, with the DH view) for any obvious intrathoracic problems, such as pleural and pericardial effusion, that could increase patient risk when restrained. The final AFAST view ends at the most gravity-dependent region, the respective umbilical view, where abdominocentesis can be performed (after completing the AFAST) if effusion is detected.

The AFAST target-organ approach

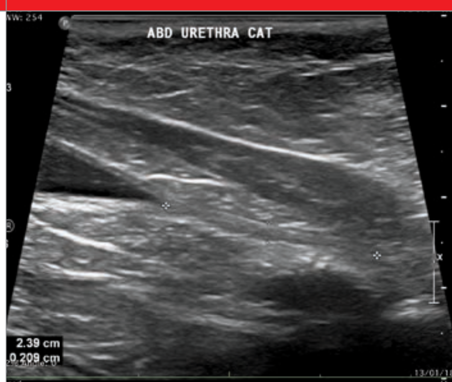
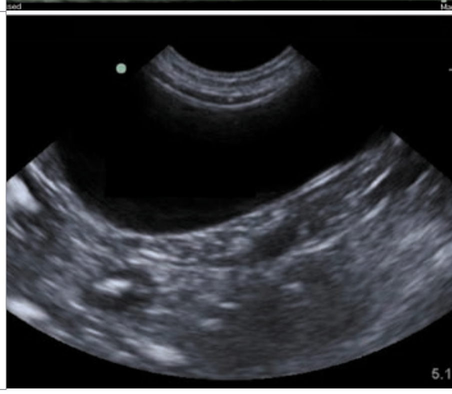
AFAST allows for sonographic assessment of easily recognized urinary tract-related conditions. The sonographer merely has to decide whether the urinary bladder is unremarkable or abnormal, and when abnormal, direct further imaging and a more streamlined approach for definitive diagnosis. Achievable abnormal AFAST findings are detailed in **Table 1**. The normal appearance of the bladder and abdominal urethra are demonstrated in **Table 2**.

The AFAST is performed by fanning (interrogating in longitudinal planes) followed by rocking cranially and returning to the starting point at each of the respective views. Therefore the Cysto-Colic (CC) view interrogates the urinary bladder in longitudinal planes while searching for free fluid in the gravity-dependent region termed the Cysto-Colic Pouch. Note that the feline urethra differs from that of dogs, in that it has a substantial length which may be imaged intra-abdominally. The Spleno-Renal (SR) and Hepato-Renal (HR) views provide soft tissue information on the left and right kidneys and are

Table 1. Questions to be asked with the AFAST Cysto-Colic View.

Question	Notes
Is there any free fluid in the abdominal (peritoneal) cavity?	Yes or no
How much free fluid in the abdominal cavity using the AFAST-applied Fluid Scoring System?	Score 0, ½ (≤ 5 mm) or 1 (> 5mm)
What does the urinary bladder look like?	Unremarkable or abnormal
What does the urinary bladder lumen look like?	Unremarkable or abnormal
What does the urinary bladder wall look like?	Unremarkable or abnormal
Is the patient intact reproductively?	Yes or no
Could I be misinterpreting an artifact or pitfall for pathology?	Know pitfalls and artifacts

Table. 2. It is vital that the clinician is familiar with the normal appearance of the feline bladder and abdominal urethra before identifying potential abnormalities.

Finding	Classic ultrasound appearance	
Normal abdominal urethra		Both the bladder and urethra should be easy to recognize during AFAST. The feline species has a significant track of abdominal urethra that may be imaged and marked by calipers. Intra-abdominal fluid-associated urethral distension may be readily appreciated if present.
Normal urinary bladder		The feline urinary bladder is generally oval-shaped, with a normal wall thickness < 2.3 mm, independent of the degree of distension (6). The bladder wall should be smooth and uniform with sonographic striation seen as a hyperechoic, hypoechoic, hyperechoic pattern.

used to search for free retroperitoneal and peritoneal fluid, and are also important for complete first-line evaluation of the feline urinary tract. This part of the assessment (which can be performed with the animal standing or in lateral or sternal recumbency) will be covered in the subsequent paper.

The AFAST CC view allows the urinary bladder to be surveyed for not only the presence, but also the degree, of sediment, which is especially helpful in urinary tract disease and urinary obstructed felines. Monitoring the amount of sediment can be helpful to assess the subsequent response to therapy (including dietary interventions), and – in cats with urinary obstruction – the degree of sediment helps determine the need for bladder lavage. Other possible findings include the presence of thrombi (blood clots), cystic calculi, bladder wall abnormalities and the location of a urinary catheter when placed. **Table 3** illustrates some of the most useful normal and abnormal findings that can be detected using this technique.

Bladder obstruction, ascites and retroperitoneal effusion

Cats with urinary obstruction commonly have ascites associated with the obstruction (6,11,12) and retroperitoneal effusion. In the most detailed study to date (to the author's knowledge) ~60% of obstructed cats were positive for pericystic fluid (analogous to the AFAST CC View) and ~35% were positive for retroperitoneal effusion (6). It is important to be aware that the clinical course for the great majority of such cats is unaltered, in that with standard care the ascites and retroperitoneal effusion will resolve in time as the patient recovers (6). Sampling and testing the effusion may support a diagnosis of uroabdomen, but medical therapy, rather than surgical intervention, is appropriate in such cases. There is speculation as to why the effusion develops in such cases, but the author proposes that it is caused by tissue inflammation and backpressure of urine against the urinary bladder wall and renal capsule (13). Using the abdominal fluid scoring (AFS) system with the AFAST-applied technique provides not only an objective semi-quantification of the volume (usually scored between 0-4, although the system can be modified for smaller volumes), but also specifies positive and negative regions (1,14-16). The scoring system provides distinct advantages over use of subjective terms such as trivial, mild, moderate and severe (which have been employed to describe the fluid), and allows monitoring of affected cats as necessary, including during daily patient rounds and recheck evaluations. From the author's experience, the free fluid usually resolves 24-36 hours after the obstruction is removed and the patient successfully resuscitated.

"Ultrasound measurements offer a non-invasive option to calculate urinary bladder volume and, with serial measurements over time, estimation of urine output. This provides important clinical information, especially in cats at risk for, or in, renal failure."

Gregory Lisciandro

Sampling accessible free fluid

When free fluid is detected on ultrasound scan and is safely accessible it must be sampled to accurately characterize it; fluid analysis and cytology should be performed to better direct care and diagnostics. When urinary tract rupture is suspected, it is helpful to compare serum creatinine or potassium levels to that of the effusion. Importantly, ultrasound cannot accurately characterize free fluid, and with larger volume effusions abdominocentesis is generally performed immediately after competing AFAST at its most gravity-dependent umbilical view, where free intra-abdominal fluid is pocketed.

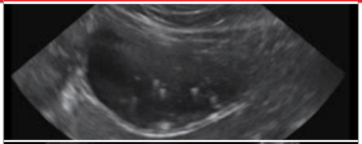
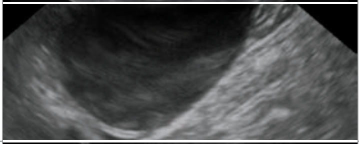
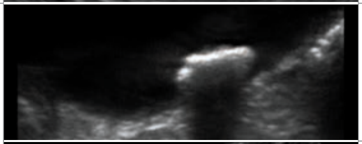
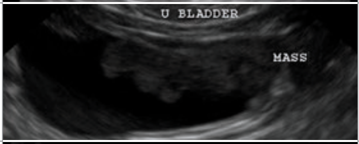
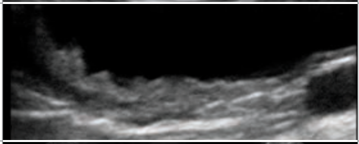
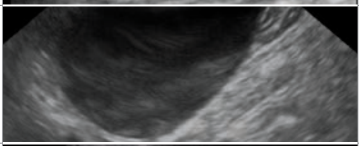
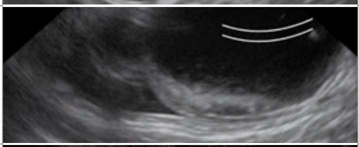
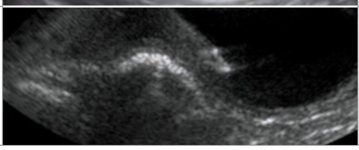
Urinary bladder volume estimation

The use of longitudinal (sagittal) and transverse measurements with the AFAST CC view can provide estimations for urinary bladder volume and, with serial measurements over time, assessment of urine output (17). The bladder is measured in longitudinal orientation at its largest oval for the measurements of length (L) and height (H) in centimeters. The probe is then rotated 90 degrees for the measurement of width (W). The formula of L x H x W x 0.625 gives an estimation of the bladder volume in milliliters **(Figure 3)**. This provides an indirect non-invasive option to gain this important clinical information, especially in cats at risk for or in renal failure.

Bladder masses

A not-uncommon scenario in small animal practice is when the veterinarian detects a suspect bladder mass when performing cytocentesis on a cat. Such cases should be staged with GFAST, partly in order to provide a much better dialogue with the client. Two simple scenarios can illustrate the point:

Table 3. Ultrasound findings of the feline urinary bladder and urethra.

Finding	Classic ultrasound appearance	
Sediment	 	Sediment is usually easy to identify using AFAST. Normal feline urine may have some degree of echogenicity (unlike the dog, where only anechoic is considered normal) because cats concentrate their urine. Often the echogenicity is due to lipid droplets; this can be normal. Urinalysis is required to definitively determine whether the urine is normal or abnormal. The second image shows the urinary bladder and a small degree of free fluid in the Cysto-Colic Pouch where the urinary bladder wall and abdominal muscle meet (anechoic triangulation). The bladder lumen has marked slice-thickness artifact that mimics sediment. Turning down the gain, ballottement, and changing the patient position are maneuvers to better differentiate one from the other. Clinicians should be aware that slice-thickness artifact can be mistaken for sediment or other pathology.
Sediment – Linear strands and septa		In this view the sediment is organized with linear strands of debris; in more severe cases actual septa form. In urinary obstructed cats, the finding of either linear strands or septa still carries a good prognosis (6).
Sediment – Sand		Different degrees of mineralized urine sediment can develop in cats. In this image the "sand" is great enough to cause distal acoustic shadowing. Clean distal acoustic shadowing is a hallmark for mineralization; small mineralized foci may be detected using color Doppler and the "twinkle artifact" (7,8).
Cystoliths (cystic calculi)		There is a single cystolith visible in this scan; note the suspect is within the urinary bladder lumen and has clean acoustic shadowing. Again care is needed; air-filled small intestine and colon can mimic cystic calculi. Ultrasound is comparable in accuracy to double contrast cystography for detection of uroliths (9).
		There are multiple cystoliths present in this image. Note the suspects are within the urinary bladder lumen and each has clean acoustic shadowing. Clean distal acoustic shadowing is a hallmark for mineralized calculi but radiography can be used to confirm AFAST sonographic suspicions.
		A loop of gas-filled intestinal tract can mimic a cystolith, as shown here. Ballottement and changing patient position can better differentiate one from the other sonographically.
Thrombus (blood clot)		Echogenic material in the bladder lumen can be due to a thrombus (blood clot). To differentiate between a neoplastic mass and a thrombus, apply color Doppler – a thrombus or blood clot should not demonstrate blood flow.
Bladder mass		A bladder wall mass: to differentiate between a mass (pulsatile flow) and a thrombus (no flow) apply color Doppler (see "Thrombus" above). Note that slice-thickness artifact may be mistaken for a mass effect if the clinician makes a hasty interpretation of the scan.
Bladder wall irregularities		An example of polypoid cystitis, showing as irregularities to the bladder wall. Remember that normal wall thickness in a moderately distended bladder is < 2.3 mm (6).
Free peritoneal fluid		The presence of small volumes of free intra-abdominal fluid (ascites) may be easily recognized in the Cysto-Colic (CC) Pouch, the most gravity-dependent region. This is also where sediment and cystoliths will settle within the urinary bladder lumen.
Urinary catheter		A urinary catheter may be imaged directly or (if having difficulty) located by moving the catheter while imaging, or gently flushing the catheter with sterile saline. It is seen as a hyperechoic (bright white) "equal sign" or parallel lines for near and far walls of the urinary catheter and/or shadowing.
Cystocentesis		The needle may be tracked using ultrasound while performing cystocentesis. Ultrasound-guided procedures are becoming standard of care in human medicine because they limit complications (10).

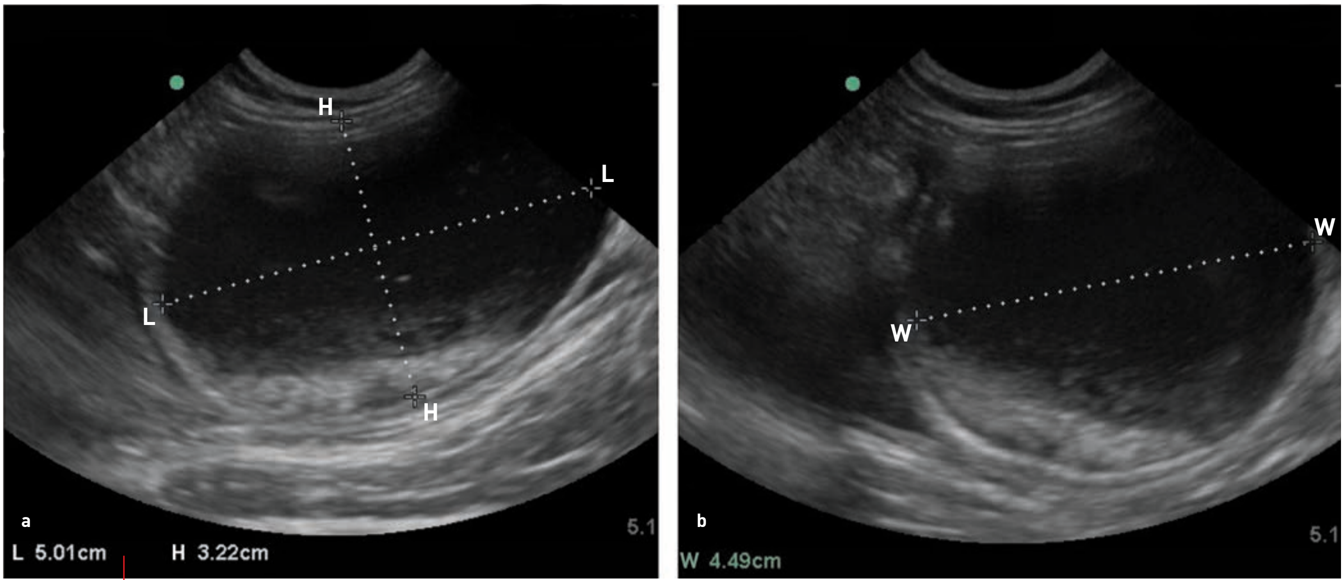


Figure 3. Urinary bladder measurements during AFAST at the Cysto-Colic View for bladder volume estimation. The bladder is measured in longitudinal orientation at its largest oval for length (L) and height (H) in centimeters (cm) **(a)**. The probe is then rotated 90 degrees to transverse orientation for the largest oval to measure width (W) **(b)**. The formula of L x H x W x 0.625 = estimation of urinary bladder volume in milliliters (mL) (18). The measurements here are 5.01 (cm) x 3.22 (cm) x 4.49 (cm) x 0.625 = 45.3 mL. These images were taken from a male cat with urinary obstruction; note that the bladder contains a substantial amount of sediment and that there is free intra-abdominal fluid adjacent to its apex in the Cysto-Colic Pouch.

(i) The clinician discovers a bladder mass during cystocentesis, aborts the procedure and returns to tell the client that there is bad news, *i.e.*, that there is likely a neoplastic process, and that an expensive work-up is recommended. If the cat is stable, the client may opt to go home to "think about it", and does not return for the work-up. This leads to a setback in the veterinarian – client relationship and can leave the client guilt-ridden at home, wondering what the best option should be for their cat.

(ii) The clinician discovers a bladder mass but returns to the exam room having already performed a GFAST assessment. The dialogue may be more upbeat than the first scenario if the scan suggests that the mass appears to be localized, with no obvious renal pelvic dilation or masses detected, no liver masses, no lung masses (from a Vet BLUE scan) and no pleural or pericardial effusion. If the cat is cooperative, TFAST echo views may also allow detection of unremarkable heart chambers. The clinician can then recommend that appropriate further tests are the next step. Conversely, if serious findings are detected on the scan, such as lung nodules (18), then the clinician should move to discuss palliative care, helping both client and pet as best as possible. Using the GFAST approach, the veterinarian-client bond becomes even stronger.

GFAST for assessing patient volume status

The feline species as a whole seems to be more susceptible to fluid volume overload, including cats with urinary obstruction (19); this may result in pulmonary edema, hepatic venous congestion, pleural or pericardial effusion, or any combination of the above (20). Obtaining a baseline GFAST on such patients on presentation is invaluable. The integration of findings during TFAST and Vet BLUE are helpful in determining if left- versus right-side volume overload is occurring. Moreover, and importantly, echo views are not needed in many patients, as the so-called "fallback views" can be sufficient. Left-sided congestive heart overload/failure results in cardiogenic lung edema and is either readily detected and scored using Vet BLUE or excluded (20-22). Right-sided congestive

"Any urinary bladder scan should be surveyed for not only the presence, but also the degree, of sediment; this technique is especially helpful with urinary tract disease and obstructed cats. Monitoring the amount of sediment can aid assessing the subsequent response to therapy."

Gregory Lisciandro

heart overload/failure results in hepatic venous congestion, which again can be readily detected by characterizing the size of the caudal vena cava and its associated hepatic veins. Moreover, pleural and pericardial effusion can occur concurrently with either condition and this can be assessed during TFAST (15,23-26). Integration of echo findings during TFAST, the characterization of the caudal vena cava, and lungs during Vet BLUE increase the probability of an accurate assessment (3).

Recording the results

Goal-directed templates are imperative to clearly convey objectives and for recording patient data that may be measured and compared initially and with future studies. Published examples may be accessed through the website FASTVet.com (1,15,27,28).

CONCLUSION

Abdominal ultrasound scans using a standardized approach should be the clinician's first-line imaging choice when presented with a cat that has potential bladder disease or abdominal trauma cases. Using the AFAST method, with defined acoustic windows with specific, consistent probe maneuvers allows targeted organ interrogation and should permit rapid assessment of cases and appropriate ongoing treatment as necessary.

REFERENCES

1. Lisciandro GR. The Abdominal FAST^3 (AFAST^3) Exam. In: Lisciandro GR (ed), *Focused Ultrasound Techniques for the Small Animal Practitioner*. Ames: Wiley-Blackwell; 2014;17-43.
2. Lisciandro SC. Focused or COAST^3 – Urinary Bladder. In: Lisciandro GR (ed). *Focused Ultrasound Techniques for the Small Animal Practitioner*. Ames: Wiley-Blackwell; 2014;99-109.
3. Lisciandro GR, Armenise AA. Focused or COAST^3: Cardiopulmonary resuscitation (CPR), Global FAST (GFAST^3), and the FAST-ABCDE Exam. In: Lisciandro GR (ed), *Focused Ultrasound Techniques for the Small Animal Practitioner*. Ames: Wiley-Blackwell; 2014;269-285.
4. Narasimhan M, Koenig SJ, Mayo PH. A whole-body approach to point of care ultrasound. *Chest* 2016;150(4):772-776.
5. Ha YR, Toh HC. Clinically integrated multi-organ point-of-care ultrasound for undifferentiated respiratory difficulty, chest pain, or shock: a critical analytic review. *J Intensive Care* 2016; 4:54. doi: 10.1186/s40560-016-0172-1.
6. Nevins JR, Mai W, Thomas E. Associations between ultrasound and clinical findings in 87 cats with urethral obstruction. *Vet Radiol Ultrasound* 2015;56(4): 439-447.
7. Gliga ML, Chirila CN, Podeanu DM, *et al*. Twinkle, twinkle little stone: an artifact improves the ultrasound performance! *Med Ultrason* 2017;19(3):272-275.
8. Simon JC, Sapozhnikov OA, Krieder W, *et al*. The role of trapped bubbles in kidney stone detection with the color Doppler ultrasound twinkling artifact. *Phys Med Biol* 2018;63(2):0205011. doi: 10.1088/1361-6560/aa9a2f.
9. Weichselbaum RC, Feeney DA, Jessen CR, *et al*. Urocystolith detection: comparison of survey, contrast radiographic and ultrasonographic techniques in an *in vitro* bladder phantom. *Vet Radiol Ultrasound* 1999;40(4):386-400.
10. Peabody CR, Manadavia D. Deep needle procedures: improving safety with ultrasound visualization. *J Patient Saf* 2017;13(2):103-108.
11. Hall J, Hall K, Powell LL, *et al*. Outcome of male cats managed for urethral obstruction with decompressive cystocentesis and urinary catheterization: 47 cats (2009-2012). *J Vet Emerg Crit Care* 2015;25(2):256-262.
12. Reineke EL, Thomas EK, Syring RS, *et al*. The effect of prazosin on outcome in feline urethral obstruction. *J Vet Emerg Crit Care* 2017;27(4):387-396.
13. Cooper ES, Owens TJ, Chew DJ, *et al*. A protocol for manging urethral obstruction in male cats without urethral catheterization. *J Am Vet Med Assoc* 2010;237(11): 1261-2166.
14. Lisciandro GR, Lagutchik MS, Mann KA, *et al*. Evaluation of an abdominal fluid scoring system determined using abdominal focused assessment with sonography for trauma in 101 dogs with motor vehicle trauma. *J Vet Emerg Crit Care* 2009;19(5):426-437.
15. Lisciandro GR. Abdominal and thoracic focused assessment with sonography for trauma, triage, and monitoring in small animals. *J Vet Emerg Crit Care* 2011;21(2):104-122.
16. Lisciandro GR, Fosgate GT, Romero LA, *et al*. Abdominal FAST (AFAST) and abdominal fluid scores in adult and juvenile cats. Abstract, *J Vet Emerg Crit Care* 2015;25(S1):S8.
17. Lisciandro GR, Fosgate GT. Use of AFAST Cysto-Colic View urinary bladder measurements to estimate urinary bladder volume in dogs and cats. *J Vet Emerg Crit Care* 2017;27(6):713-717.
18. Kulhavy DA, Lisciandro GR. Use of a lung ultrasound examination called Vet BLUE to screen for metastatic lung nodules in the emergency room. Abstract, *J Vet Emerg Crit Care* 2015;25(S1);S14.
19. Ostroski CJ, Drobatz KJ, Reineke EL. Retrospective evaluation of and risk factor analysis for presumed fluid overload in cats with urethral obstruction: 11 cases (2002-2012). *J Vet Emerg Crit Care* 2017;27(5):561-568.
20. Ward JL, Lisciandro GR, Keene BW, *et al*. Accuracy of point-of-care lung ultrasound (Vet BLUE protocol) for the diagnosis of cardiogenic pulmonary edema in dogs and cats with acute dyspnea. *J Am Vet Assoc* 2017;250(6):666-675.
21. Lisciandro GR, Ward JL, DeFrancesco TC, *et al*. Absence of B-lines on lung ultrasound (Vet BLUE protocol) to rule out left-sided congestive heart failure in 368 cats and dogs. Abstract, *J Vet Emerg Crit Care* 2016;26(S1):S8.
22. Lisciandro GR, Fulton RM, Fosgate GT, *et al*. Frequency and number of B-lines using a regionally-based lung ultrasound examination in cats with radiographically normal lung compared to cats with left-sided congestive heart failure. *J Vet Emerg Crit Care* 2017;27(3):267-277.
23. Lisciandro GR, Lagutchik MS, Mann KA, *et al*. Accuracy of Focused Assessment with Sonography for Trauma (TFAST) to detect pneumothorax in 145 dogs with blunt and penetrating trauma. *J Vet Emerg Crit Care* 2008;18(3):258-269.
24. Lisciandro GR. Evaluation of initial and serial combination focused assessment with sonography for trauma (CFAST) examinations of the thorax (TFAST) and abdomen (AFAST) with the application of an abdominal fluid scoring system in 49 traumatized cats. Abstract, *J Vet Emerg Crit Care* 2012;22(S2):S11.
25. Lisciandro GR. The use of the diaphragmatico-hepatic (DH) views of the abdominal and thoracic focused assessment with sonography for triage (AFAST/TFAST) examinations for the detection of pericardial effusion in 24 dogs (2011-2012). *J Vet Emerg Crit Care* 2016;26(1):125-131.
26. McMurray J, Boysen S, Chalhoub S. Focused assessment with sonography in nontraumatized dogs and cats in the emergency and critical care setting. *J Vet Emerg Crit Care* 2016;26(1):64-73.
27. Lisciandro GR. The Thoracic FAST^3 (TFAST^3) Exam. In: Lisciandro GR (ed), *Focused Ultrasound Techniques for the Small Animal Practitioner*. Ames: Wiley-Blackwell; 2014;140-165.
28. Lisciandro GR. The Vet BLUE Lung Scan. In: Lisciandro GR, (ed). *Focused Ultrasound Techniques for the Small Animal Practitioner*. Ames: Wiley Blackwell; 2014;166-187.

HOW I APPROACH... UROLITHIASIS AND SPECIFIC GRAVITY IN CATS

Prevention and treatment of urolithiasis in our feline patients requires a multi-factorial approach; here Cecilia Villaverde reviews one of the most important aspects, namely maintenance of a low urinary specific gravity, and suggests possible ways to achieve this.

Cecilia Villaverde,

BVSc, PhD, Dipl. ACVN, Dipl. ECVCN Expert Pet Nutrition, Fermoy, Co. Cork, Ireland

Dr. Villaverde obtained her veterinary degree and her PhD from the Universitat Autònoma de Barcelona and then completed a residency in small animal nutrition at the University of California Davis. She is board certified in veterinary nutrition by both the American College of Veterinary Nutrition and the European College of Veterinary and Comparative Nutrition, and is a recognized European Specialist in Veterinary and Comparative Nutrition. Dr. Villaverde is currently a consultant for Expert Pet Nutrition and the Veterinary Information Network (VIN).

KEY POINTS

1. Urolithiasis in cats can result in morbidity and even mortality for affected animals; the most common uroliths in cats are struvite and calcium oxalate.
2. Promoting urine dilution is one of the strategies recommended for all types of uroliths, with an aim of achieving a consistent urine specific gravity of 1.030 or lower.
3. Urine dilution can be promoted by various methods, including feeding high moisture diets or adding water to food to increase total water intake.
4. The use of sodium-enriched diets in some situations may be appropriate to help promote diuresis.

Introduction

Urolithiasis is one of the most frequent causes of feline lower urinary tract disease (FLUTD). The most common uroliths in cats (more than 80-90%) are struvite (magnesium ammonium phosphate) and calcium oxalate, according to those submitted for analysis (1,2). Struvite stones were the most commonly reported urolith type until the mid-1990's, but this has changed over time and currently calcium oxalate is the most frequent urolith found on analysis, with an incidence of 40-50%, closely followed by struvite (1,2). The reason for the increase in calcium oxalate and the decrease in struvite stones in cats is unknown, but might be related to alterations in some commercial diets implemented to prevent struvite stone formation. Such changes include varying diet composition to ensure a reduction in the magnesium content of the food and acidification of the urine (3).

Diet is undoubtedly important for both treatment and prevention of urinary calculi, and some specifically formulated diets can promote struvite stone dissolution and reduce its recurrence (4,5). On the other hand, calcium oxalate stones cannot be medically dissolved and, although we believe diet is important for prevention, its exact role is not yet clear, and there are a lack of clinical studies assessing the effect of dietary modification on their recurrence. The American College of Veterinary Internal Medicine (ACVIM) has produced a consensus statement on the treatment and prevention of canine and feline uroliths (6), although it is noteworthy that there is not general consensus amongst all Board Certified Veterinary Nutritionists™ regarding all recommendations made in this statement. However, most experts agree that struvite stones should be medically dissolved (unless contraindicated) with dissolution foods and/or medication.

Relative Super Saturation (RSS)

Given the importance of diet for treatment and prevention of urolithiasis, it is essential to have reliable methodology to assess the effect of diet on urinary environment and composition. Crystallization – the initial step for stone formation – will occur when the urolith precursors are free (and in the correct chemical form) to react with each other, and are present in the urine at high concentration (*i.e.*, the urine is supersaturated with these precursors). However, supersaturation alone is not the only factor that affects stone formation, because cats usually have urine supersaturated in calcium oxalates (7), but only a small percentage form uroliths.

Relative supersaturation (RSS) reflects the degree of urine supersaturation for a given crystal compound and has been used as a measure of stone risk in dogs and cats. Calculation of RSS (8-10) requires feeding a chosen diet to a cohort of animals for several days, followed by total urine collection to permit volume, pH, urine specific gravity (USG) and the concentrations of several crystallizing ions to be measured **(Figure 1)**. The activity product of the crystal is compared to its solubility product using specialized software to obtain the RSS. The RSS value obtained for a given crystal will help separate the metastable from the supersaturation state.

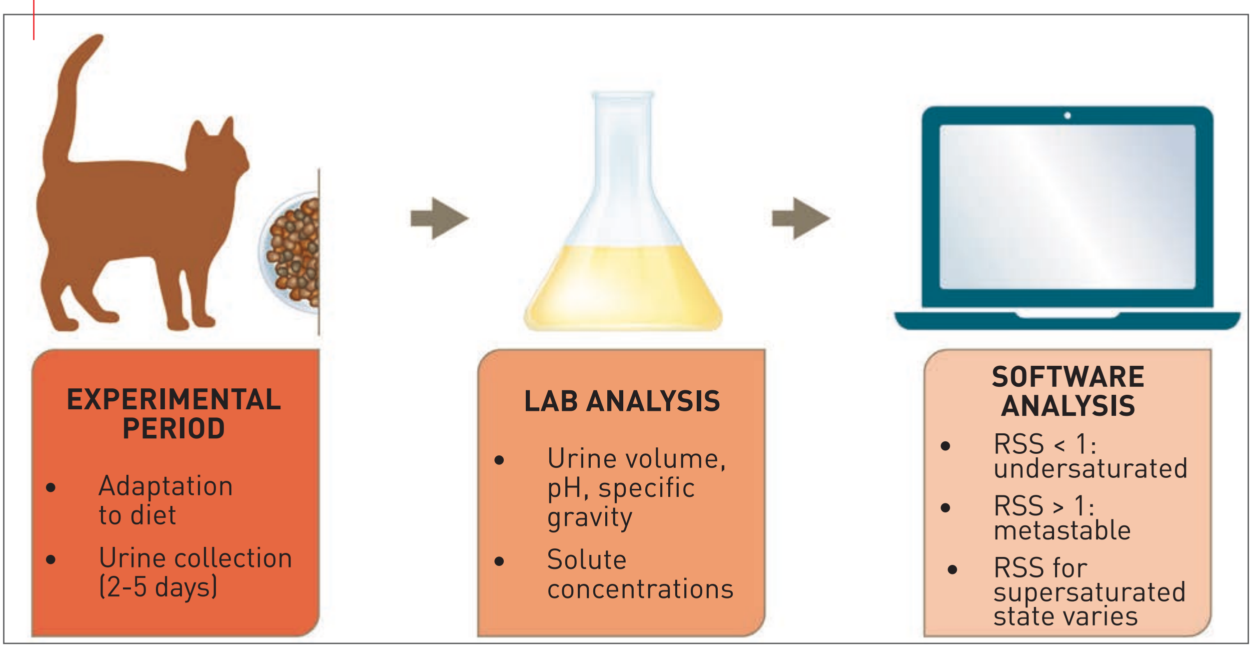
Determining RSS is costly and complex to perform, and hence has been broadly restricted to research settings. In addition, RSS values have been determined mainly in healthy cats, and it is possible that results could be different in stone formers. We should therefore be cautious when extrapolating results from healthy cats to those with stone disease.

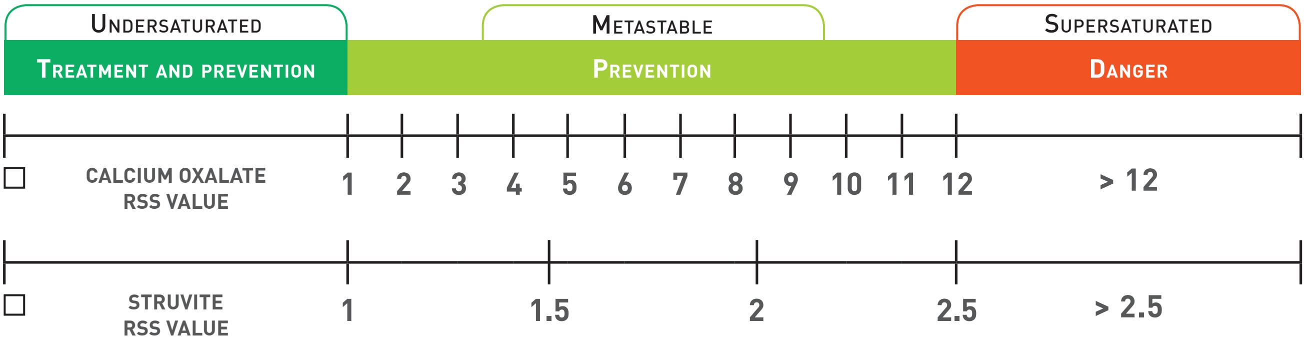
Data supports the fact that using diets promoting an RSS < 1 for struvite can result in stone dissolution (11,12) and studies suggest that RSS is a good indication of struvite dissolution dynamics (13). There is less data for calcium oxalate and for other non-struvite stones. Studies have shown that specifically formulated urinary diets can reduce the RSS for calcium oxalate into the metastable range in stone forming cats and dogs (14,15), **(Figure 2)**. This suggests that diet plays a (significant) role in decreasing the risk of recurrence of calcium oxalate stones in affected patients but additional research is needed to help determine (or confirm) if this correlates with the desired clinical output, *i.e.*, prevention or delay of recurrence (6).

Role of urine dilution in urolithiasis prevention

The degree of urine dilution is one of the factors affecting the supersaturation of urine, and increased dilution is a mainstay in the treatment of urinary stone prevention in humans. Warmer climates have been identified as a risk factor for urolithiasis (16), which could be in part related to higher water

Figure 1. Determination of relative supersaturation (RSS) for a given crystal in experimental conditions.





Stone composition	Undersaturated	Metastable	Supersaturated
Struvite[1]	Stones will dissolve	New stones will not form; existing stones will grow slowly	New stones will readily form
Calcium oxalate	Existing stones will not grow	New stones will not form; existing stones will grow slowly	New stones will readily form

[1]If a urease-producing bacterial infection is present, the infection must be appropriately treated based on urine culture and sensitivity.

Figure 2. Each of the RSS zones has different implications for the risk of urolith formation, as shown above. The table summarizes the situation for both struvite and calcium oxalate crystals.

losses. However, the etiopathogenesis of urolithiasis is complex, and it is therefore difficult to determine the importance of individual dietary modifications. There is a lack of research on the effect of promoting urine dilution by increasing water intake alone (independent of mineral content, urinary pH, and other dietary factors) but there is overall agreement that promoting urine dilution will reduce RSS and thus help reduce the risk of stone formation.

One epidemiological study – involving 173 cats with calcium oxalate uroliths, 290 cats with struvite uroliths, and 827 controls (with no urinary tract disease) – aimed to identify dietary risk factors for both struvite and calcium oxalate urolithiasis (17). They found that diets with the highest moisture content were associated with a lower calcium oxalate risk, but had no effect on struvite; however, this research has the usual limitations of retrospective studies, and other diet modifications might have affected these results. There are no prospective clinical studies on the effect of urine dilution alone in clinical outcome for stone forming cats.

The increased urine volume associated with urine dilution can help prevent stone formation by both reducing the concentration of precursors **(Figure 3)** and by increasing the frequency of urination, resulting in reduced mineral retention time in the urinary tract. Many review papers propose urine dilution/increased urine volume as one of the steps to prevent stone recurrence (3,18). Many clinicians recommend that management of uroliths, independent of their composition, requires urine dilution to reduce or prevent recurrence, and (as noted above) the aim is to achieve a USG of 1.030 or below in a consistent manner (6). In my experience, it is advisable to warn owners that the goal is actually to cause polyuria, and the litter box might require more frequent cleaning once strategies to decrease USG have been implemented.

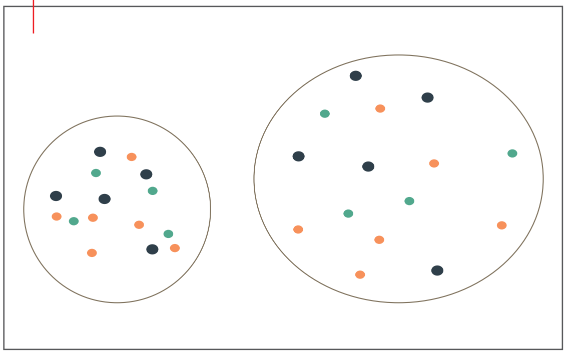
How to achieve urine dilution

Cats have the remarkable ability to concentrate their urine when fed diets low in moisture and/or have limited access to water; USG values of 1.065 and above have been reported (18). Compared to dogs, it is harder to achieve urine dilution in cats due to this potent concentration capability, but I will consider several options to promote water intake and subsequent urine dilution **(Figure 4)**.

Increase dietary water

One of the safest methods is to increase water consumption by using canned high moisture foods or by adding water to dry food; this latter method can be a cost-effective alternative to purchasing wet diets. Studies have shown that high moisture intake increases urine volume and decreases USG (19,20). One study (21) involved six healthy cats which were

Figure 3. It can be helpful to use a simple diagram to illustrate to owners how urine dilution will reduce the concentration of solutes and thus decrease the likelihood of crystallization.



fed 4 different diets; this consisted of the same base diet but with variable amounts of water added (to give a total moisture content of 6.3%, 25.4%, 53.3% and 73.3%). The diets were fed for three weeks on a crossover design, and water intake, urine production, USG, and RSS were assessed for each cat. The researchers found that increasing dietary moisture resulted in a decrease in consumption of drinking water. However, cats fed the highest moisture diet (73.3%) consumed more water overall (drinking water plus dietary water) compared to the other three diets. When the cats were fed this diet it resulted in a higher urine volume over a 24-hour period (86.7 mL on average) compared to the other diets. Moreover, the diet with the highest moisture resulted in lower USG (1.036 on average) compared to the other diets (1.052-1.054) and a decreased RSS for calcium oxalate, whereas there was no effect of diet on struvite RSS.

Another study (14) involved ten cats with calcium oxalate stones which had been fed various diets with differing nutrient composition but with a moisture content ranging from 9-18%. The cats were switched to a canned urinary diet with 78% moisture content. This tended to increase urine volume and decrease USG, and resulted in a significant decrease in calcium oxalate RSS. However, there were multiple differences between the original diets and the trial diet, and so the effects may be due to a combination of different dietary factors.

It has been recommended that urinary diets should have a moisture content of at least 75% (8). In my experience, aiming for a dietary moisture of 85% **(Box 1)** helps achieve a consistently low USG throughout the day, especially in recurrent cases.

Not all cats will tolerate the addition of water on top of the food, so it is important to introduce this slowly, or to use high moisture diets that provide more than 80% moisture for these animals.

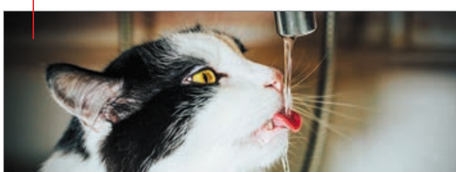
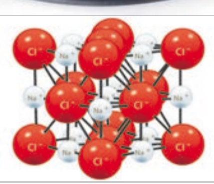
Dry diets can also reduce the RSS for struvite and calcium oxalate (7) in the urine of healthy cats by modification of other dietary factors affecting stone formation, such as pH and concentration of precursors and inhibitors. Some dry diets may also result in lower RSS by using methods other than water intake to promote diuresis, such as salt-enriched diets.

It is important to be aware that adding water changes a diet's palatability and texture that can lead to a cat refusing to eat. It also reduces energy density, which may cause unwanted weight loss in normal weight or thin cats, or those with picky appetites. If water is added to kibble this can lead to spoilage if the food remains in the bowl for any length of time, and softening the kibble can also mean that the dental benefit (*i.e.*, mechanical scrubbing of the teeth) is lost.

Use high sodium diets

Some dry diets formulated for feline urolithiasis have higher levels of sodium (up to 3.5 g/1000 kcal) than average maintenance diets (which are around 1 g/1000 kcal or less). High sodium foods can promote urine dilution by stimulating diuresis (22). The retrospective study mentioned previously that assessed dietary risk factors for feline struvite and calcium oxalate urolithiasis (17) identified that diets lower in sodium had a higher risk for calcium oxalate stone formation. Again, the result has

Figure 4. A summary of methods that can promote water intake and urine dilution.

	**Stimulate water intake** • Fresh clean water • Multiple water stations • Use running water (water fountains, etc.)
	**Use wet foods** • Moisture level > 70% • Some wet foods have moisture level > 80% • Additional water can be added to wet foods to achieve desired goal
	**Add water to diet** • Gradual introduction to promote acceptance • Typical amount: 2 cups of water per cup of dry food (adjust according to goals) • It can be blenderized together to make a slurry if direct water addition is not palatable to cats
	**Use salt-enriched diets** • If cat/owners do not accept wet diets • Do not use if salt-sensitive diseases are present

Box 1. An example of how to calculate the amount of water to be added to food to achieve a desired moisture content; here the aim is to achieve a moisture content of 85% for both dry and canned food.

Goal moisture content is 85% = 85 grams of water per 100 grams of food
To re-calculate moisture once water is added to 100 grams of food, the formula is as follows, where x indicates the mL (or grams) of water added to 100 g of food

85% total moisture = [% moisture diet + x/100 g + x] x 100

Example with a dry diet (10% moisture)

85% = [10% + x/100 g + x] x 100
85/100 = [10 + x/100 + x]
0.85(100 + x) = 10 + x
85 + 0.85x = 10 + x
75 = 0.15x
500 = x

Per 100 grams of dry food, add 500 mL (approx. 2 cups) of water (1:5 weight, 1:2 volume)

Example with a wet diet (70% moisture)

85% = [70% + x/100 g + x] x 100
85/100 = [70 + x/100 + x]
0.85(100 + x) = 70 + x
85 + 0.85x = 70 + x
15 = 0.15x
100 = x

Per 100 grams of wet food, add 100 mL of water (1:1 volume)

to be taken with caution, since this correlation can be affected by other factors and does not imply causation.

A long-term study in cats – conducted over a two-year period – assessed the effect of a high sodium diet (3.1 g/1000 kcal) vs. a control diet (1 g/1000 kcal) on renal parameters, blood pressure and urinary parameters (23). The treatment diet did not negatively affect renal parameters or blood pressure, and it did decrease USG compared to the control diet, but only at the 3-month mark, which suggests that the effect of high salt diets on promotion of diuresis might not be sustained long term. One abstract (24) reported a positive effect on urine volume with a high salt diet fed to healthy cats after two weeks, but no differences were detected on USG or RSS for calcium oxalate or struvite; these results were similar to another study, also with healthy cats and of three weeks' duration (25). Both studies were short term and involved only a small number of cats.

The high sodium approach cannot be used in cats with salt-sensitive diseases (*e.g.*, renal or cardiac pathologies) out of caution, and it is not to be recommended for urate or cystine stones. There is concern about high sodium diets promoting calciuria, but short-term data in healthy cats (25) suggest that even though renal calcium excretion can increase, urinary calcium concentration might remain unaffected due to the concurrent effect of salt on increasing urine volume.

It is important to obtain more prospective research on the effect of sodium-enriched diets on USG, RSS, other urinary parameters, and clinical outcomes. Whilst the ACVIM consensus statement recommends the use of high moisture diets over high sodium diets (6), these may be an option when clients cannot afford, or refuse the use of, high moisture diets.

Promote drinking water intake

Common advice to clients with stone-forming cats includes promotion of water intake. This may be achieved by using running water (such as water fountains), flavored water, additional water bowls/stations, and the use of specific materials for the water bowl (26). I find that flavoring water with a maximum of 15 mL of fluid – using either water from cans of tuna or chicken broth (homemade or, if commercial, without garlic or onion) – per 500 mL bowl can be successful. However, there is a lack of research supporting the efficacy of these measures on urine dilution and on clinical outcomes. The effect of different water presentation systems on the RSS of calcium oxalate and struvite, USG, urine osmolality and urine volume of colony cats has been assessed (27). The methods compared were: still, circulating, and free-falling bowl systems, which were used for two weeks in a crossover design study. There were no differences in RSS, average water intake, urine volume or USG. Osmolality was higher in cats where circulating water was offered compared to still or free-falling. Moreover, the lowest USG found in the study was 1.044, which is still too high for stone prevention.

This study failed to show that the use of water fountains can affect urine dilution. However, some of the cats in the study showed a strong preference for a specific bowl, thus it is important to offer different options to our patients to identify individual preferences. This also applies to the material and shape of the drinking container. The water bowl(s) should be placed in a clean, odorless location, and separate from the litter tray and food. Multiple water stations located in different parts of the home could potentially be helpful, and will ensure the cat has access to water at all times.

Monitoring

In cats with stone disease, long-term follow-up is important to minimize recurrence. At the very least, this will allow for early detection of uroliths and the

"Flavoring the drinking water may encourage cats to increase their water intake, but there is a lack of research as to how effective this is on urine dilution and the eventual clinical outcomes."

Cecilia Villaverde

use of relatively non-invasive methods for stone removal if necessary. The frequency and the type of tests performed for the follow-up (urinalysis, imaging, culture, etc.) will vary depending on the individual case (type of stone, association with infection, co-morbidities, previous episodes, etc.) and the client's budget.

With regard to urine dilution, the most common method used in daily practice is measuring USG with a refractometer; dipstick measures of USG are unreliable. Owners can purchase a refractometer, or the clinician can perform this test with urine obtained by the client, with non-absorbable litter employed for urine collection at home. The first assessment should be 4-6 weeks after the preventative measures have been started. The urine should always be obtained at the same time of day for each follow-up, since USG will vary over a 24-hour period; for example, the first urine of the day can be more concentrated than samples taken later in the afternoon.

If the USG is not in the desired range (*i.e.*, < 1.030), it is important to check compliance with the recommended treatment (diet, medications, addition of water, etc.). If compliance is good, the use of a diet with higher moisture than the current one (or adding more water on top) is indicated until the USG is within the acceptable range. If not previously attempted, owners should be encouraged to use more than one water station and figure out the preferred drinking method of their cat (*i.e.*, size and material for the bowl, still or running water, flavored or non-flavored water).

CONCLUSION

Diet choice in cats with stone disease will vary depending on the specific stone, goal (dissolution vs. prevention), presence of co-morbidities, previous episodes, and client finances. However, in all cases the diet chosen should promote urine dilution, either by being high moisture or (if not contraindicated) high in salt. If the diet does not meet either requirement, water should be gradually added to the diet. For all strategies, I advocate a slow introduction to maximize acceptance and avoid common problems of sudden diet transition, such as diarrhea. Long-term regular monitoring of the urine is mandatory to ensure the patient's health remains optimal. Ultimately, however, it is important to recognize that RSS is still very much the most critical factor for controlling stone formation in cats, and any program designed to aid an at-risk patient must be holistic in its nature.

REFERENCES

1. Cannon AB, Westropp JL, Ruby AL, *et al*. Evaluation of trends in urolith composition in cats: 5,230 cases (1985-2004). *J Am Vet Med Assoc* 2007;231(4):570-576.
2. Houston DM, Vanstone NP, Moore AE, *et al*. Evaluation of 21,426 feline bladder urolith submissions to the Canadian Veterinary Urolith Centre (1998-2014). *Can Vet J* 2016;57:196-201.
3. Palm C, Westropp J. Cats and calcium oxalate: strategies for managing lower and upper tract stone disease. *J Feline Med Surg* 2011;13:651-660.
4. Smith DM, Weese HE, Evason MD, *et al*. A diet with a struvite relative supersaturation less than 1 is effective in dissolving struvite stones *in vivo*. *Br J Nutr* 2011;106 Suppl 1:S90-S92.
5. Luich JP, Kruger JM, Macleay JM, *et al*. Efficacy of two commercially available, low-magnesium, urine-acidifying dry foods for the dissolution of struvite uroliths in cats. *J Am Vet Med Assoc* 2013;243:1147-1153.
6. Lulich JP, Berent AC, Adams LG, *et al*. ACVIM Small Animal Consensus Recommendations on the Treatment and Prevention of Uroliths in Dogs and Cats. *J Vet Intern Med* 2016;30:1564-1574.
7. Smith BH, Stevenson AE, Markwell PJ. Urinary relative supersaturations of calcium oxalate and struvite in cats are influenced by diet. *J Nutr* 1998;128:2763S-2764S.
8. Stevenson AE, Wrigglesworth DJ, Smith BH, *et al*. Effects of dietary potassium citrate supplementation on urine pH and urinary relative supersaturation of calcium oxalate and struvite in healthy dogs. *Am J Vet Res* 2000;61:430-435.
9. Markwell PJ, Smith BHE. An effective urine pH monitoring system for cats. *Anim Tech* 1993;44: 239-245.
10. Robertson WG, Jones JS, Heaton MA, *et al*. Predicting the crystallization potential of urine from cats and dogs with respect to calcium oxalate and magnesium ammonium phosphate (struvite). *J Nutr* 2002;132:1637S-41S.
11. Houston DM, Weese HE, Evason MD, *et al*. A diet with a struvite relative supersaturation less than 1 is effective in dissolving struvite stones *in vivo*. *Br J Nutr* 2011;106 Suppl 1:S90-S92.
12. Torres-Henderson C, Bunkers J, Contreras ET, *et al*. Use of Purina Pro Plan Veterinary Diet UR Urinary St/Ox to dissolve struvite cystoliths. *Top Companion Anim Med* 2017;32:49-54.
13. van Hoek I, Malandain E, Tournier C, *et al*. RSS is a better predictor for struvite dissolution than urine pH. *Vet Focus* 2009; 9(2):47-48.
14. Lulich JP, Osborne CA, Lekcharoensuk C, *et al*. Effects of diet on urine composition of cats with calcium oxalate urolithiasis. *J Am Anim Hosp Assoc* 2004;40:185-191.
15. Stevenson AE, Blackburn JM, Markwell PJ, *et al*. Nutrient Intake and Urine Composition in Calcium Oxalate Stone-Forming Dogs: Comparison with Healthy Dogs and Impact of Dietary Modification. *Vet Ther* 2004;5(3):218-231.
16. Gomes VDR, Ariza PC, Borges NC, *et al*. Risk factors associated with feline urolithiasis. *Vet Res Commun* 2018;42:87-94.
17. Lekcharoensuk C, Osborne CA, Lulich JP, *et al*. Association between dietary factors and calcium oxalate and magnesium ammonium phosphate urolithiasis in cats. *J Am Vet Med Assoc* 2001;219:1228-1237.
18. Bartges JW, Callens AJ. Urolithiasis. *Vet Clin North Am Small Anim Pract* 2015;45:747-768.
19. Deng P, Iwazaki E, Suchy SA, *et al*. Effects of feeding frequency and dietary water content on voluntary physical activity in healthy adult cats. *J Anim Sci* 2014;92:1271-1277.
20. Thomas DG, Post M, Bosch G. The effect of changing the moisture levels of dry extruded and wet canned diets on physical activity in cats. *J Nutr Sci* 2017;6:e9.
21. Buckley CM, Hawthorne A, Colyer A, *et al*. Effect of dietary water intake on urinary output, specific gravity and relative supersaturation for calcium oxalate and struvite in the cat. *Br J Nutr* 2011;106 Suppl 1:S128-S130.
22. Nguyen P, Reynolds B, Zentek J, *et al*. Sodium in feline nutrition. *J Anim Physiol Anim Nutr* 2017;101:403-420.
23. Reynolds BS, Chetboul V, Nguyen P, *et al*. Effects of dietary salt intake on renal function: a 2-year study in healthy aged cats. *J Vet Intern Med* 2013;27:507-515.
24. Xu H, Laflamme DP, Bartges JW, *et al*. Effect of dietary sodium on urine characteristics in healthy adult cats. *J Vet Intern Med* 2006;20:738.
25. Paßlack N, Burmeier H, Brenten T, *et al*. Short-term effects of increasing dietary salt concentrations on urine composition in healthy cats. *Vet J* 2014;201:401-405.
26. Larsen JA. The role of water in disease management. In; *Proceedings* ACVIM Forum 2018; access online.
27. Robbins MT, Cline MG, Bartges JW, *et al*. Quantified water intake in laboratory cats from still, free-falling and circulating water bowls, and its effects on selected urinary parameters. *J Feline Med Surg* 2018 [Epub ahead of print].

HOW I APPROACH... FELINE IDIOPATHIC CYSTITIS

Feline idiopathic cystitis is one of the most common problems encountered in small animal practice. Isabelle Demontigny-Bédard reviews the condition and in particular discusses the behavioral aspects that should be considered when dealing with these cases.

Isabelle Demontigny-Bédard,

DVM, DES, MSc, Dipl. ACVB, DMV Veterinary Center, Montreal, Canada

Dr. Demontigny-Bédard obtained her Doctorate in Veterinary Medicine from the Faculty of Veterinary Medicine, Université de Montréal in 2010. She completed a residency in behavior at the same faculty in 2014 and was board-certified by the American College of Veterinary Behaviorists in 2015. She recently concluded a Master's degree on feline pica behavior and is currently a veterinary behavior specialist in Montreal and with the Passionimo network.

KEY POINTS

1. **Feline idiopathic cystitis is a condition involving the lower urinary tract, not a medical condition of the lower urinary tract.**
2. **Feline idiopathic cystitis occurs when a susceptible cat is exposed to internal or external stress.**
3. **Treating this condition involves introducing various environmental modifications aimed at reducing stress.**
4. **Medical therapy may be necessary to treat idiopathic cystitis but this should always be in conjunction with introduction of appropriate measures to address the specific risk factors involved.**

Introduction

The intermittent presence of dysuria, stranguria, hematuria, pollakiuria and/or periuria with no identifiable medical cause in a cat may be consistent with feline idiopathic cystitis, or FIC. This is also the most frequent condition that produces clinical signs related to the lower urinary tract in this species. Feline idiopathic cystitis occurs when a susceptible cat is exposed to internal or external stress, and it is increasingly accepted that FIC is a condition involving the lower urinary tract, rather than a *medical* condition of the lower urinary tract.

Pathophysiology

Bladder abnormalities

In healthy cats, the urothelium is protected by a layer of glycosaminoglycans (GAGs), but in cats with FIC, the excretion of GAGs in urine is decreased (1). If the GAG layer and/or the urothelium are compromised, there may be contact between substances in the urine and the sensory nerves of the bladder, which could lead to neurogenic inflammation (2). Increased permeability of the bladder is also documented in cats with FIC (3).

Neuroendocrine abnormalities

An increase in the immunoreactivity of tyrosine hydroxylase has been noted in the *locus coeruleus* and the paraventricular nucleus of the hypothalamus in cats with FIC **(Figure 1)** (4). Tyrosine hydroxylase is a rate-limiting enzyme in the conversion of tyrosine to catecholamines such as norepinephrine. Cats with FIC therefore produce more catecholamines and have higher circulating catecholamine levels than unaffected cats (5), with a resultant over-activation of the sympathetic branch of the nervous system. Furthermore, chronic stimulation of the alpha-2 receptors of the *locus coeruleus* leads to their desensitization, adversely affecting their role in inhibiting the release of catecholamines, which contributes to the inflammatory response (2).

As FIC symptoms are often related to exposure to stressors, it is interesting to note that cats with FIC exhibit suboptimal activation of the hypothalamic-pituitary-adrenal (HPA) axis. Indeed, one study reported that administration of exogenous corticotropin-releasing hormone did not cause an increase in ACTH and cortisol in cats with FIC (6). Another study reported that the adrenal glands in cats with FIC were smaller than in normal cats (7).

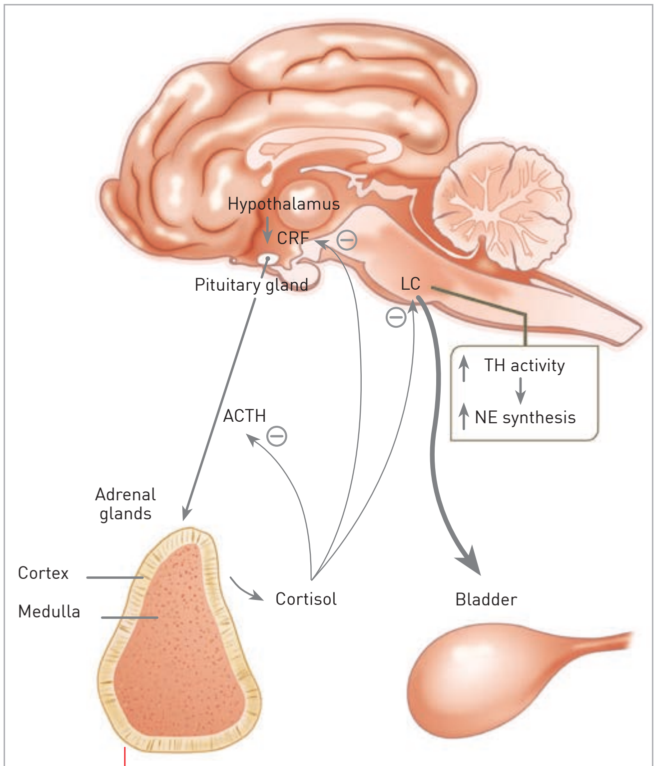


Figure 1. Neuroendocrine abnormalities have been reported in cats with FIC, namely under-activation of the HPA axis and over-activation of the sympathetic nervous system.**TH =** tyrosine hydroxylase – **NE =** norepinephrine – **CRF** = corticotropin-releasing factor – **LC** = *locus coeruleus*

Risk factors

The identified risk factors for FIC vary from one study to another, but certain elements are highlighted in several sources. Overall, affected cats tend to be middle-aged, overweight males (8). Environmental risk factors, such as living entirely indoors, being a low-activity cat, and residing in a dwelling with multiple cats, have also been identified (8). Conflict with other cats, moving house, or being nervous or scared are also elements recognized as risk factors (8).

Diagnosis

FIC is a diagnosis of exclusion. The main differential diagnoses are urolithiasis, a behavioral problem such as marking or urinating in the house, or a urinary tract infection. Once I have compiled a case history, I move on to basic diagnostic procedures, which include a physical examination, urinalysis and abdominal X-rays. For cases which are recurrent or persistent, ultrasound of the urinary tract should be considered. At the initial consultation, I usually recommend complementing the urinalysis with hematology, biochemistry, and total T4 measurements. If diagnostic procedures do not reveal any abnormality, or simply identify bladder inflammation, a more detailed case history **(Table 1)** should be obtained to determine if FIC risk factors are present and to identify possible sources of stress in the patient's environment.

Table 1. Pointers when taking a case history.

Known health issues and treatments
Known behavioral issues and treatments
Any changes in behavior
Excessive or decreased grooming

Lifestyle
• Outside access
• Activity level
• Structured periods of interaction with the owner
• Presence of other animals (indoors and outside)
  • Cats
  • Dogs
  • Interactions

Access to resources • High places to climb and rest • Food and water areas • Litter box • Food dispensing toys and other toys • Rotation/use of any toys
Reactions to usual and unusual stimuli • Startling • Hiding • Acting aggressively
Changes in routine and environment • Moving house • New family member • Change in schedule • Change in furniture • Renovation work
Litter box care

Treatment

The treatment plan for FIC may vary from one cat to another, and should involve identifying possible sources of stress for the affected individual and what

Table 2. Characteristics of environmental elements that could activate a stress response.

Characteristic	Examples
Unpleasant sensory elements	Cold temperatures, rough surfaces, loud noises, unpleasant or strong odors
Newness	Unfamiliar person, moving house
Inconsistency with cat's expectations	Change in schedule, delay in meal times, unpredictability in litter box cleaning
Inability for cat to control its surroundings	No places to hide or climb, forced or inappropriate handling, inability to show normal behavior

"The treatment plan for a patient with idiopathic cystitis will depend on the individual animal, but should involve identifying possible sources of stress for the affected cat and what is required to reduce or eliminate these sources."

Isabelle Demontigny-Bédard

is required to reduce or eliminate these sources **(Table 2)**. When treating this condition I focus on introducing environmental modifications aimed at reducing stress. One study looked at the occurrence of gastrointestinal, urinary or dermatological diseases and abnormal behavior in cats with FIC and normal cats over a period of 77 weeks (9). Any changes in routine or the environment were noted; these included variations in the care routine, lack of contact with the habitual carer or being cared for by unfamiliar individuals, altered feeding routine, lack of playtime and lack of environmental enrichment in the cage. Exposure to such types of changes significantly increased the relative risk of having partial anorexia, of not toileting for 24 hours, and of defecating and urinating outside the litter box. This was seen equally in cats with FIC and normal cats. In a controlled and enriched environment, it seems to be possible to get FIC-prone cats to have no further episodes of clinical signs or abnormal behavior compared to normal cats (9). This is why it is so important to put a maximum of effort into reducing possible sources of stress for cats with FIC.

The Indoor Pet Initiative at The Ohio State University is an excellent and free online resource for both owners and animal health professionals to help achieve this goal (10). Stress suffered by or affecting an individual animal is on a continuum, *i.e.*, it is cumulative. The goal is to allow the cat to remain below the reactivity or illness threshold for a given individual. To do so, a *multimodal environmental modification* (MEMO) approach has been shown to be effective (11). It includes the elements that are addressed below.

Optimal litter box care

When trying to create the "perfect bathroom" for a cat, there are four main categories that I consider: substrate, tray, cleanliness and location **(Table 3)**. Without doubt individual preferences may exist, but most cats will have similar standards.

For the substrate, a clumping, unscented, finely textured litter is recommended. The bottom of the litter box tray should be covered with at least 5 centimeters of litter.

Litter boxes must be large. Most authors suggest that they should be at least 1.5 times the cat's size, from the tip of the nose to the base of the tail. The cat must be able to fully enter the litter box, turn around and scratch while extending its legs, but most commercial litter boxes do not meet these standards. I often recommend using large storage bins, such as those designed to fit under beds; these provide a sufficiently large surface area, yet the edge is not too high for the cat to step over it. Some owners are more creative and will use other types of containers **(Figure 2)**. If owners choose storage bins with a high edge, I suggest they cut an opening in one side for easy access. Litter boxes must also be changed annually, as plastic is a porous material.

Most authors recommend uncovered litter boxes; however, at least one study has reported that this does not make a real difference to most cats (12). Rather, it seems that the location of the litter box, its cleanliness and the substrate are more important for most cats than the presence or absence of a cover. Nevertheless, I tend to recommend uncovered litter boxes, as it seems that owners generally care for them more when waste is visible or smells are more obvious. Finally, if there is more than one cat, the number of litter boxes should be sufficient so that one individual

Table 3. Checklist for optimal litter box care.

Substrate	• Clumping • Unscented • Fine texture • ⩾ 5 cm thick
Box	• Size: 1.5 times the cat's size • Used for less than one year • Number of trays = number of cats + 1
Cleanliness	• Daily removal of waste • Full cleaning at least monthly • Full cleaning with hot water and dish soap
Location	• Easy to access • Area with little disturbance • ⩾ 1 box per floor • In different rooms

Figure 2. Litter boxes must be large but a variety of options are available – for example, a child's sandbox can be used.

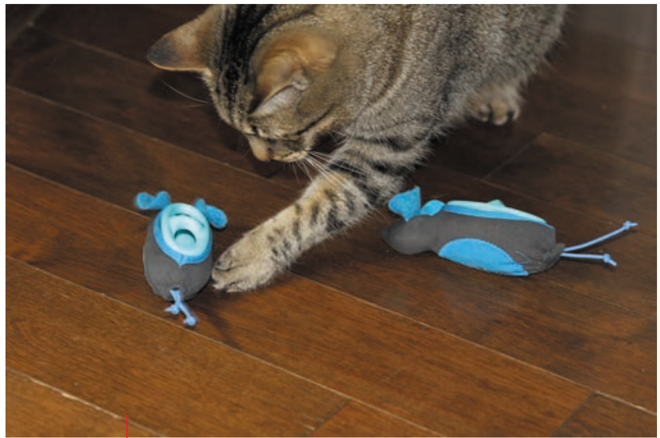


Figure 3. Food-dispensing toys can help mimic natural feeding behavior by encouraging a cat to work for its food and explore its environment.

cannot block access to the litter boxes. This is the reason for the frequent recommendation that the number of litter boxes be equal to the number of cats plus one.

Cleanliness of the litter tray is a key element, and waste must be removed daily. Experience indicates that the element owners most frequently neglect is thoroughly cleaning the litter box. This should be done at least once a month when clumping litter is used and more frequently for non-clumping litter. This involves discarding the litter, cleaning the litter box with warm water and soap, and refilling it with new litter once dry.

Finally, the trays should be both easily accessible and located in areas with little disturbance. In houses with two or more floors, at least one litter box should be placed on each floor. Also, multiple litter boxes in the same room only count as one litter box; as far as access is concerned, there is no real benefit to having more than one litter box in the same room.

Space

Three-dimensional space is important for felines, and cats should be offered plenty of space that enables them to express normal behaviors. It is therefore wise to offer several choices of high places for cats to climb and rest. In households with more than one cat, I believe it is essential that some of these structures should be sized for just one cat; this means that if one cat is already occupying a perch, it is more difficult for another individual to come and dislodge the occupant.

Stable scratching posts, made with a variety of materials and high enough for cats to scratch while stretching, should be accessible near resting areas. Indeed, many cats scratch when getting up after a period of rest.

Cats are predators that hunt small prey in the wild, and numerous attempts at hunting end up in failure. Therefore the time indoor cats spend feeding should reflect this, and food-dispensing toys that encourage cats to work for food and explore their environment are particularly interesting. Preferences vary from one cat to another, and it is wise to rotate the items used to maintain interest and an adequate level of mental stimulation. Some toys involve more movement, while others are more static but require greater use of their paws **(Figure 3)**.

It is important to ensure that each cat can access all resources at all times, especially in multi-cat households. Therefore, several places should be provided for eating, drinking, resting, scratching, etc. Cats that live together should not be forced to cross paths or use the same resource at the same time unless they want to. It is wise to have all these resources on each floor of a house, even in a household with only one cat. As such, if a cat needs to toilet, it does not necessarily need to climb stairs to access the litter tray and meet its needs. The same applies if visitors are present; the cat should be able to stay within its comfort zones if it does not want to interact with strangers.

Predictability and routine

As mentioned above, small alterations in routine can be sufficient to cause changes in appetite and elimination for cats, and can even result in inappropriate toileting. Therefore, having the most stable schedule and environment possible is recommended. If changes must take place, this should be gradual wherever possible. For example, if a dietary change must be made, it is recommended to continue to offer the current diet at the usual feeding place whilst introducing the new diet at the same location. Gradually, owners can give less and less of the usual diet and more and more of the new diet.

Structured and predictable interactions with owners should be prioritized. To achieve this goal, punishment should be avoided; in fact, punishment can increase stress and weaken the human-animal bond. I recommend that my clients identify their cat's favorite interactions with them and set aside periods for such interactions at the same time each day. For example, a brushing session in the morning after breakfast, then a play session with a toy on a stick after work, and petting in the evening before bedtime.

Diet and water consumption

Many diets are designed to help maintain urinary health for cats, but to date studies have not definitively shown that such diets will help in all cases of FIC. When treating such cases I tend to focus more on water intake than dietary composition, although I will always ensure that the cat is being fed a balanced diet. I encourage owners to increase the cat's water intake, and will often recommend that canned (wet) food is offered wherever possible, as it can result in a lower recurrence of FIC (8,13,14). The use of water fountains is often recommended for cats with FIC, although one study noted that this did not result in a statistically significant increase in water intake with a group of cats; however, clear individual preferences for how the water was offered were noted (15). It therefore seems wise to offer both a water fountain and a water bowl to a cat to discover its preferences.

Medication

Because FIC is self-limiting, pharmacological therapy aims to improve the patient's comfort during an active episode. I consider drugs such as buprenorphine (as it can be administered under the tongue at home by cat owners), or gabapentin can be useful in some cases, as it has an effect on neurogenic pain and anxiety. However, neither drug is licensed for treating FIC. Studies have shown that amitriptyline is not recommended for acute management of FIC (16,17), but is effective in decreasing the clinical signs of recurrent FIC (18).

If intercat aggression has been identified as a source of stress, it must also be addressed, and medication may be required. If a cat with FIC has been the victim of aggression from another cat, the victim is not necessarily the one that should be medicated; in fact if this type of aggression is identified, it is usually the aggressor who is exhibiting the abnormal behavior. It is therefore common for the aggressor to require appropriate pharmacological treatment and behavioral therapy in order to address the problem at source and thereby reduce stress to the victim. However, sometimes the victim will also benefit from concurrent pharmacological therapy to reduce stress or anxiety.

In certain cases, despite optimal litter box care, plentiful surroundings, maintaining a routine, proper diet and addressing aggression, it will be clear that a cat with FIC still shows signs of fear or anxiety. In such cases, the use of psychotropic medication may help to keep the animal's stress level low enough to help decrease the recurrence of FIC, and fluoxetine, a selective serotonin reuptake inhibitor, is one of my top choices for treating anxiety in cats. The fluoxetine dose that I use is 0.5-1.0 mg/kg PO once daily, but I always start at the low end of the dosage range and increase progressively if necessary.

CONCLUSION

FIC can become a source of frustration for owners, especially if they do not fully understand what is happening. As animal health professionals, we should be clear that, thanks to current knowledge, FIC should no longer be regarded as a urinary tract problem. Owners have far greater power than they realize to decrease the recurrence of FIC; they can, with our support, change the cat's environment to make this possible. If, despite all their efforts in this regard, their cat cannot cope with the residual sources of stress, a pharmacological treatment may help, but it is far better to address the environmental factors first.

REFERENCES

1. Buffington CT, Blaisdell JL, Binns Jr SP, *et al*. Decreased urine glycosaminoglycan excretion in cats with interstitial cystitis. *J Urol* 1996;155:1801-1804.
2. Hostutler RA, Chew DJ, DiBartola SP. Recent concepts in feline lower urinary tract disease. *Vet Clin North Am Small Anim Pract* 2005;35:147-170.
3. Lavelle JP, Meyers SA, Ruiz WG, *et al*. Urothelial pathophysiological changes in feline interstitial cystitis: a human model. *Am J Physiol Renal Physiol* 2000;278:F540-F553.
4. Reche Jr A, Buffington CT. Increased tyrosine hydroxylase immunoreactivity in the *locus coeruleus* of cats with interstitial cystitis. *J Urol* 1998;159:1045-1048.
5. Westropp JL, Kass PH, Buffington CAT. Evaluation of the effects of stress in cats with idiopathic cystitis. *Am J Vet Res* 2006;67:731-736.
6. Buffington CT, Pacak K. Increased plasma norepinephrine concentration in cats with interstitial cystitis. *J Urol* 2001;165:2051-2054.
7. Westropp JL, Welk KA, Buffington CT. Small adrenal glands in cats with feline interstitial cystitis. *J Urol* 2003;170:2494-2497.
8. Forrester SD, Towell TL. Feline idiopathic cystitis. *Vet Clin North Am Small Anim Pract* 2015;45:783-806.
9. Stella JL, Lord LK, Buffington CT. Sickness behaviors in response to unusual external events in healthy cats and cats with feline interstitial cystitis. *J Am Vet Med Assoc* 2011;238:67-73.
10. The Ohio State University – Indoor Pet Initiative Web site. Environmental Enrichment Resources and References. Available at: https://indoorpet.osu.edu/veterinarians/environmental-enrichment-resources-and-references. Accessed Jan 23, 2019.
11. Buffington CT, Westropp JL, Chew DJ, *et al*. Clinical evaluation of multimodal environmental modification (MEMO) in the management of cats with idiopathic cystitis. *J Feline Med Surg* 2006;8:261-268.
12. Grigg EK, Pick L, Nibblett B. Litter box preference in domestic cats: covered versus uncovered. *J Feline Med Surg* 2013;15:280-284.
13. Markwell PJ, Buffington CA, Chew DJ, *et al*. Clinical evaluation of commercially available urinary acidification diets in the management of idiopathic cystitis in cats. *J Am Vet Med Assoc* 1999;214:361-365.
14. Markwell PJ, Buffington CT, Smith BH. The effect of diet on lower urinary tract diseases in cats. *J Nutr* 1998;128:2753S-2757S.
15. Pachel C, Neilson J. Comparison of feline water consumption between still and flowing water sources: a pilot study. *J Vet Behav* 2010;5:130-133.
16. Kraijer M, Fink-Gremmels J, Nickel RF. The short-term clinical efficacy of amitriptyline in the management of idiopathic feline lower urinary tract disease: a controlled clinical study. *J Feline Med Surg* 2003;5:191-196.
17. Kruger JM, Conway TS, Kaneene JB, *et al*. Randomized controlled trial of the efficacy of short-term amitriptyline administration for treatment of acute, non-obstructive, idiopathic lower urinary tract disease in cats. *J Am Vet Med Assoc* 2003;222:749-758.
18. Chew DJ, Buffington CA, Kendall MS, *et al*. Amitriptyline treatment for severe recurrent idiopathic cystitis in cats. *J Am Vet Med Assoc* 1998;213:1282-1286.

EARLY SCREENING FOR FELINE HEMATURIA

Early screening for feline hematuria is now possible using a new product which can be added to cat litter, offering a unique tool for the management of lower urinary tract disease in cats.

KEY POINTS

1. **Lower urinary tract diseases (LUTD) in cats are frequent, progressive and recurrent pathologies, but they are not always detected by owners.**

2. **Macroscopic or microscopic hematuria is almost always present during LUTD, which makes it a good early potential biomarker for these pathologies.**

3. **The *Hematuria Detection* screening test* can reliably and rapidly detect microhematuria and is therefore a useful tool in the management of LUTD.**

4. **Recent recommendations have been developed for the use of this product in managing feline urinary disorders.**

Introduction

A non-invasive test to screen for feline hematuria has just been launched on the market and is now available in many countries. Easy to use and stress-free, it consists of formulated white granules which, when sprinkled onto cat litter, will quickly turn blue on contact with hemoglobin **(Figure 1)**. The granules will detect early cases of microhematuria, *i.e.*, before macroscopic hematuria has developed. This short paper details the relevance of this monitoring tool, the operating principle underlying the test, the product reliability studies, and possible recommendations for use when dealing with urinary disorders.

Hematuria and feline LUTD

Hematuria is defined as the presence of an abnormal number of red blood cells (RBC) in the urine: it can be microscopic (occult) or macroscopic (visible). Generally, "pathological" hematuria is defined as five or more red blood cells per field at high microscopic magnification.

Although the causes of hematuria are numerous, in cats it is perhaps most frequently encountered with lower urinary tract disease (LUTD), a frequent presentation in small animal clinics (1). The term LUTD covers a group of pathologies characterized by certain clinical signs: hematuria, dysuria,

Figure 1. The granules turn a distinctive blue color when they come into contact with hemoglobin.

© Blücare Lab

* Marketed by Royal Canin as *Hematuria Detection*, except in Canada where it is sold as Blücare®.

Elodie Khenifar,

DVM, MSc. Candidate, Intersand and Blücare Laboratories, Boucherville, Quebec, Canada

Dr. Khenifar graduated from the National Veterinary School of Toulouse in 2013 and worked in both large and small animal practice for two years before moving to Quebec in 2016 to study for a MSc. in pathology and microbiology. She has served as Veterinary Science Liaison at Intersand and Blücare Lab since 2017.

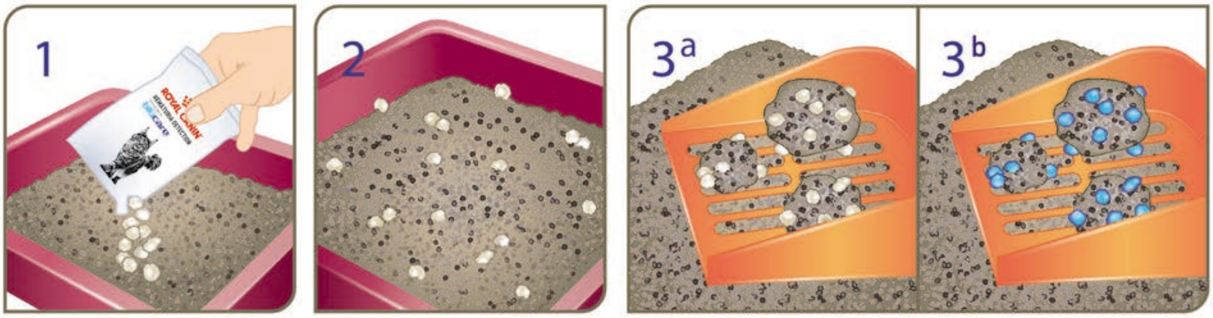


Figure 2. The instructions for using the product are straightforward.

stranguria, pollakiuria and/or periuria, progressing to include various systemic signs if urethral obstruction develops.

When presented with a cat that has LUTD, the main differential diagnoses are feline idiopathic cystitis, urolithiasis, urethral plugs, and urinary tract infection (1). Lower urinary tract pathologies are subject to relapses even when appropriate treatment is administered: overall, 50% of cats that have had an LUTD episode will have a recurrence at some point (2).

Monitoring of hematuria in managing LUTD

During an episode of urinary disease, hematuria is almost always present, at least in microscopic form (1). Since cats frequently do not demonstrate obvious pain, they are often only presented to the veterinarian when the problem has advanced to a significant level, for example with a urethral blockage or following numerous episodes of periuria. However, given the frequency of recurrence of these pathologies, it seems appropriate to focus on an easy and non-invasive screening method for a biomarker such as microhematuria. Use of such a product will allow owners to monitor their pet regularly for signs of hematuria and should facilitate attendance at the veterinary clinic in the early stages of urinary disease.

Test operating principles

The *Hematuria Detection* test is composed of small white granules which are sprinkled on the cat litter. The granules contain 3,3', 5,5'-tetramethylbenzidine (TMB), a molecule that imparts a blue color to the granules via a pseudo-peroxidation reaction when it comes into contact with hemoglobin. The results are almost immediate; the color appears in less than a minute and remains visible for over 48 hours. The instructions for use are simple **(Figure 2)** and the product can be used by owners to monitor their cat for early signs of urinary disorders. The long shelf life of the product – 2 years in the sealed packaging – is also beneficial, and the granules remain reactive for 30 days when placed on the cat litter. Note that any type of cat litter can be used, but the owner will need to remove any granules soiled by urine each day because they will no longer be absorbent.

Clinical studies conducted by the University of Montreal have shown the granules to be extremely sensitive; the lowest reactivity threshold has been determined at 100 RBC/μL (3), corresponding

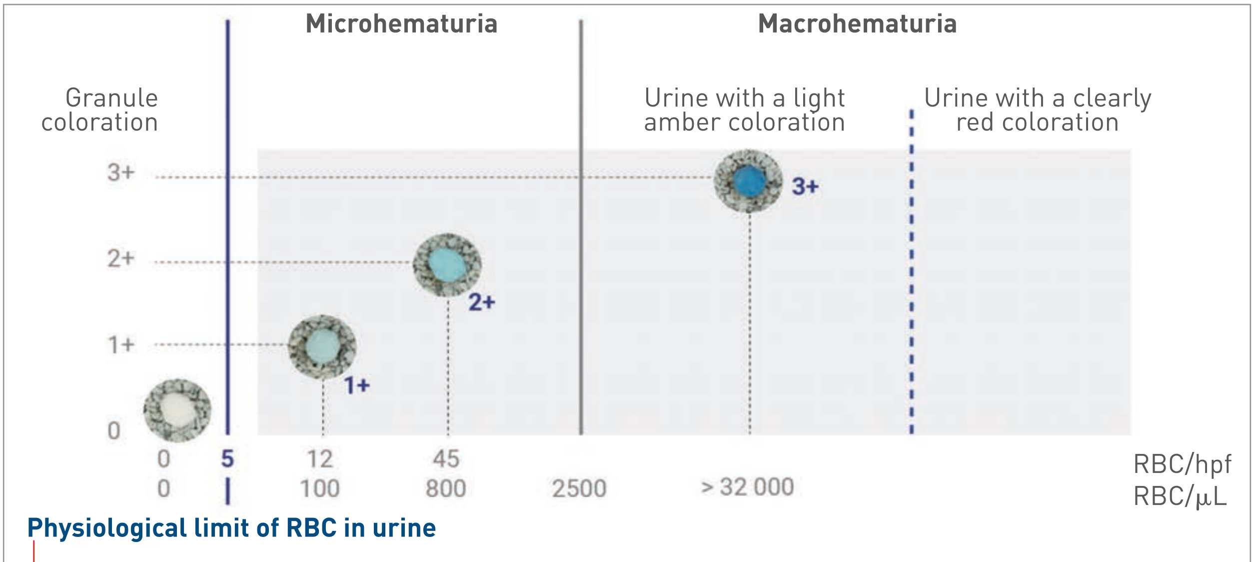


Figure 3. The coloration of the granules will vary according to the concentration of blood in the urine; the image shows the response for a urine sample at pH = 6, USG = 1.026 (4).

Table 1. Recommendations for the screening and monitoring of cats predisposed to hematuria and cats with urinary tract disease (6).

	Urinary tract disease (UTD) monitoring		
Description	Urolithiasis (upper or lower urinary tract) or urethral plugs	Idiopathic cystitis	Urinary tract infection (upper or lower)
Diet recommendations	Specific diet	Stress reducing, urinary tract diet	Life stage or specific diet
Frequency of *Hematuria Detection* usage	**ACUTE MONITORING** Monitor resolution of hematuria during treatment		
	10-14 days	5-7 days	10-14 days
	IMMEDIATE RELAPSE AND CONTINUOUS MONITORING Monitor for immediate relapse and periodically check for relapses		

to approximately 12 RBC/hpf **(Figure 3)**. Studies confirm the product has good reliability, but note that sensitivity decreases if the urine pH is ≥ 8.5 and/or urine specific gravity (USG) is above 1.050 (4). The toxicological risk for both animal and user is assessed as negligible to very low (5).

Recommendations for use

This innovative product opens up the possibility that owners can use the product on a regular basis in various situations. A group of feline specialists have drawn up recommendations for the use of the granules for monitoring acute episodes of urinary tract disease or where monitoring of urinary tract disease is required **(Table 1)**.

CONCLUSION

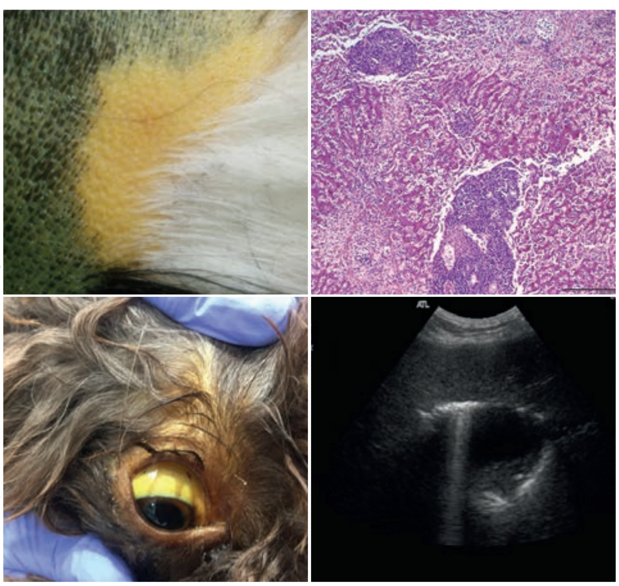
Hematuria Detection is thought to be the only test currently on the market that can detect feline microhematuria at home, directly via the litter and without the need for urine collection. The simplicity of the product means that the granules should be a useful addition for clinicians and owners when monitoring and treating cats with various forms of LUTD.

REFERENCES

1. Dorsch R, Remer C, Sauter-Louis C, *et al*. Feline lower urinary tract disease in a German cat population; a retrospective analysis of demographic data, causes and clinical signs. *Tierärztliche Praxis Ausgabe K Kleintiere Heimtiere* 2014;42(4):231-239.
2. Bartges J, Polzin DJ. Lower urinary tract disorders. In; *Nephrology and Urology of Small Animals*. Chichester, West Sussex, UK; Ames, Iowa: 2011 Wiley-Blackwell. p.750.
3. Khenifar E, del Castillo JRE, Gara-Boivin C. *Ex vivo* sensitivity and robustness of a novel home-screening test for feline hematuria. *J Feline Med Surg* 2018;20;845-859. Clinical/research abstract accepted for presentation at ISFM Congress 2018, p.854.
4. Khenifar E, del Castillo JRE, Gara-Boivin C. Reliability assessment of a novel home-screening test for feline hematuria, *J Feline Med Surg* 2018;20;845-859. Clinical/research abstract accepted for presentation at ISFM Congress 2018, p.854-855.
5. del Castillo JRE. Profil toxicologique des pastilles. *Personal communication*, November, 2017.
6. Scherk M, Buffington CAT, Carozza E, *et al*. Blücare® Granules: A novel tool for the early detection and monitoring of urinary tract disorders in cats; recommendations from an expert panel. Available at: https://www.linkedin.com/company/bl%C3%BCcare-lab/?originalSubdomain=fr Accessed Dec 15, 2018

veterinary focus #29.3

The worldwide journal for the companion animal veterinarian



© Cynthia Webster; © Carolina Naranjo (Idexx); © Jordi Puig; © Jordi Puig

COMING UP...

In our next issue, we will look at various aspects of liver and pancreatic disease.

- **Exocrine pancreatic insufficiency in dogs**
  Dolores Tabar, Spain
- **How I approach... the dog with altered hepatic enzymes**
  Jordi Puig, Spain
- **Feline diabetes mellitus**
  Christine Iben, Austria
- **Feline cholangitis**
  Craig Webb, USA
- **Chronic canine hepatitis**
  Cynthia Webster, USA
- **Canine pancreatitis – diagnostics and pitfalls**
  Iwan Burgener, Austria
- **Nutrition for feline pancreatitis**
  Karin Allenspach, USA
- **Diagnostic imaging for hepatic and pancreatic disease**
  Laurent Blond, France

ROYAL CANIN®