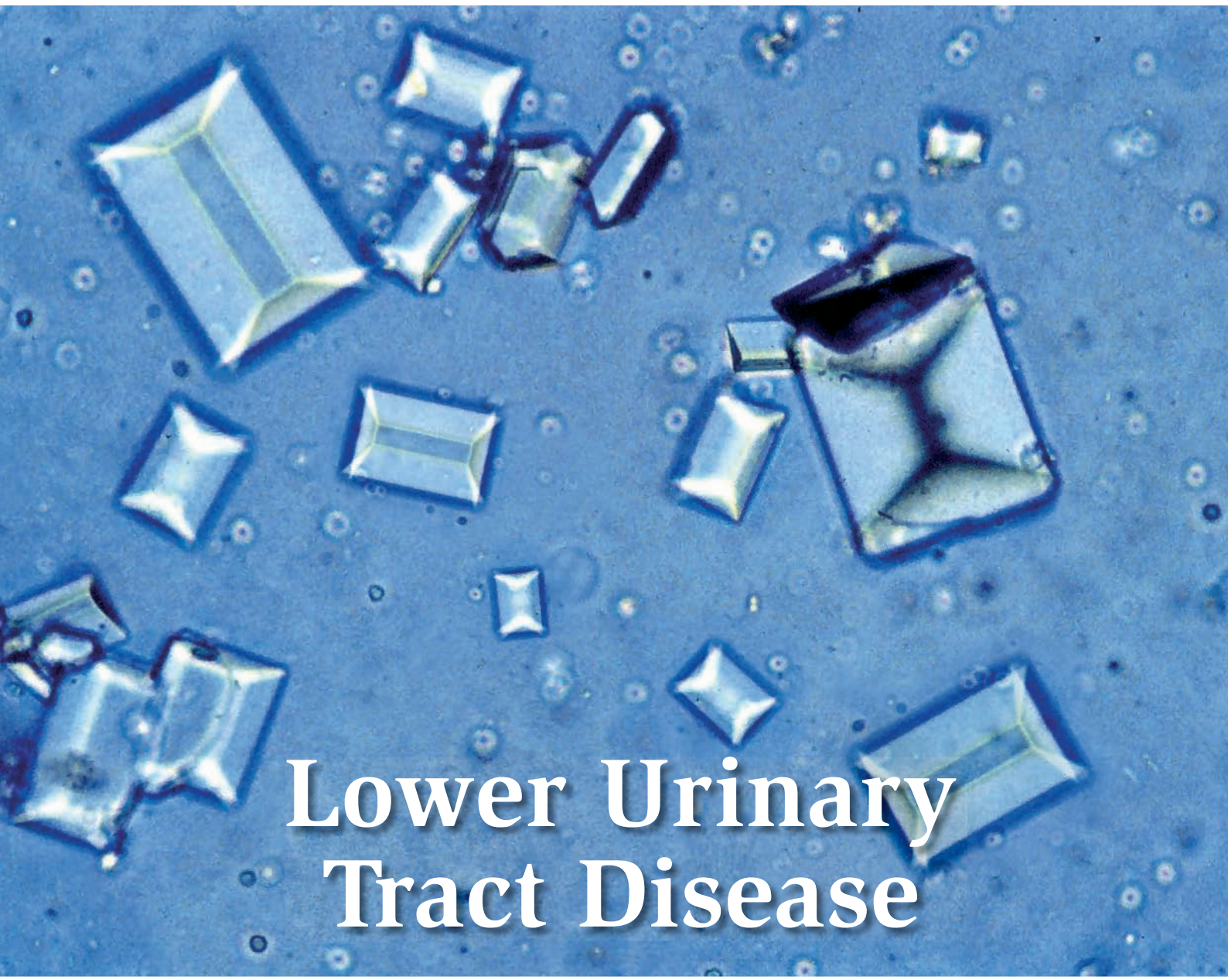
VETERINARY
focus
#24.1
2014 - $10/€10
The worldwide journal for the companion animal veterinarian



Lower Urinary Tract Disease

Urogenital defects in dogs • Urates in bladder disease • How I approach...Feline idiopathic cystitis • Epidemiology – characteristics of cats diagnosed with cystitis • Urinary relative supersaturation and urolithiasis risk • How I treat...The cat with a blocked bladder • Imaging the urinary tract • Urinalysis

ROYAL CANIN

27th ANNUAL CONGRESS OF THE ESVD-ECVD

11-13 SEPTEMBER 2014
SALZBURG-AUSTRIA

SAVE THE DATE

Scientific and Continuing Education Programme
Free communications and Posters

Conference topics:

- Otitis and middle ear disease
- Aetiology of food allergy and food trials
- What to do when it's not a cat or a dog
- MRSP
- Cytology in practice
- Practical pharmacology and drug interactions
- Compliance with treatment, and communicating effectively with clients
- Alopecia and hair cycle disorders
- Update on ectoparasite control
- Scaling
- Pathology - basic and advanced
- Journal clubs, and clinical updates
- How to get the most from a paper and how to spot cheating in clinical trials

President ESVD: Susan Paterson, UK
President ECVD: Richard Harvey, UK
President Scientific Organizing Committee: Tim Nuttall, UK
President Local Organizing Committee: Otto Fischer, Austria

ESVD - European Society of Veterinary Dermatology

ECVD - European College of Veterinary Dermatology

THE LONG-TERM PARTNERS OF ESVD/ECVD

WWW.ESVD-ECVDCONGRESS.COM

Salzburg Congress www.salzburgcongress.at

EDITORIAL

The ancient Greek physician Hippocrates is, by general consent, considered one of the outstanding figures in the history of medicine; his writings, wisdom and of course his oath - which even today serves as a basis for other, similar oaths and laws that define good medical practice and ethics - have come down to us throughout the centuries. Hippocrates and his followers laid the foundations for medicine to develop and eventually diverge into all its specialties, but two millennia ago, in an age when there was no microscope, stethoscope, or even thermometer, the tools and aids available to these primitive doctors were very limited. This probably explains why uroscopy - the practice of visually examining a patient's urine for symptoms of disease - was a central tenet of medical practice at that time, although from our viewpoint it was an archaic and unreliable means of reaching a diagnosis; many of the assumptions made by ancient physicians regarding uroscopy have proved to be not only unscientific but quite incorrect, yet for hundreds of years numerous treatises on the technique were published.

But from such false beginnings came true wisdom; one can speculate that uroscopy led eventually to urinalysis - which nowadays is a simple and readily available technique that acts as a key to open the door of diagnosis for many different diseases - and more sophisticated investigative methods and ever-advancing knowledge eventually ensured that urology became a well-developed branch of medicine, such that this issue of *Veterinary Focus* is dedicated to the urinary system and its ailments. So while times have changed, Hippocrates still reaches down over the millennia. The original Oath cautioned against surgery, stating "… (the physician) will not cut for stone, even for patients in whom the disease is manifest …(but) will apply dietetic measures for the benefit of the sick…". Can we conjecture that Hippocrates foresaw the day when we could treat many uroliths by diet alone? And as readers explore the pages ahead, they will be reminded that another of his maxims still holds good for veterinarians in the 21st century: "I will prescribe regimens for the good of my patients, according to my ability and judgment".

Ewan McNeill - Editor-in-chief

Deputy publisher: Buena Media Plus
CEO: Bernardo Gallitelli
Address: 85, avenue Pierre Grenier 92100 Boulogne - 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
- Pierre Ménard

Printed in the European Union
ISSN 1354-0157
Circulation: 80,000 copies
Legal deposit: March 2014
Cover: WCPN

Veterinary Focus is also published in French, German, Chinese, Italian, Polish, Spanish, Japanese & Russian.

ROYAL CANIN

Urogenital defects in dogs

Claudio Brovida, DVM, PhD
ANUBI® Ospedale per Animali da Compagnia, Moncalieri, Italy

Dr. Brovida graduated from the Veterinary School of Turin, Italy and developed his professional interests in small animal practice, with particular focus on internal medicine, nephrology, and urology. He is currently Director of the ANUBI® Ospedale per Animali da Compagnia in Moncalieri, where he established a hemodialysis and blood purification unit in 1996. A past President of the World Small Animal Veterinary Association (WSAVA), at present he is an active member of the International Renal Interest Society (IRIS) and the WSAVA Renal Pathology Clinical Group.

Introduction

The urinary system is formed by a coordinated development of different tissues that interact during the embryonic phase. The bladder and urethra are formed by the partitioning of the cloaca, the caudal portion of the embryonic intestine. The urorectal cavity subdivides into upper and lower sections to form the rectum and the urogenital cavity respectively.

KEY POINTS

- **Various structural anomalies can occur in the canine urogenital organs resulting in alterations to reproductive and/or urinary function.**
- **Such defects principally involve the urinary system; ectopic ureters in female dogs are the most commonly encountered problem.**
- **The most useful methods for diagnosis are various imaging modalities, such as ultrasound, contrast medium radiology, computed tomography and cystoscopy.**
- **Urinary tract infections are the most common complication seen with urogenital defects.**
- **Surgery is the preferred treatment for most urogenital anomalies.**

The urogenital cavity is linked caudally with the amniotic cavity and cranially with the allantois, part of the placenta, through the allantoic cord. The bladder subsequently develops from the proximal urachus and the cranial portion of the urogenital cavity, while the ureters develop from the caudal portion of the urogenital cavity. At birth, the urachus narrows and finally closes.

As the embryo develops, the mesonephric ducts and the embryonic ureters form separate openings in the caudal portion of the urogenital cavity. With the development of the bladder, the ureters open cranially at the level of the bladder neck, while the mesonephric ducts give rise to the proximal urethra. The mesonephric duct also forms the basis for the development of the external genital organs in the male and the vagina in the female (1,2).

A number of morphological and functional anomalies involving the urinary and genital tracts can occur in dogs, although some are rare and will only be mentioned briefly (see ***Table 1***). This article considers the most common canine urogenital anomalies encountered in clinical practice, the most appropriate procedures required to achieve a correct diagnosis, and the relevant treatment options.

Ectopic ureters

An ectopic ureter is an anatomical anomaly characterized by the fact that the distal portion of the ureter does not open correctly at the level of the bladder trigone, but rather finishes elsewhere within the urinary tract or lower genitalia; the anomaly may be either uni- or bilateral in affected animals. The pathogenesis of the condition is linked to an anomalous development or incorrect migration of the embryonic mesonephric ducts, which

Table 1. Urogenital defects in dogs (1,2,21).

Defect	Characteristics	Breed susceptibility	Gender predilection	Symptoms
Ectopic ureter	Uni- or bilateral Intra- or extra-mural	Siberian husky, Newfoundland, English bulldog, Labrador retriever, golden retriever, collie, West Highland white terrier, fox terrier, Skye terrier, toy and miniature poodles, mixed breeds	Far more common in females than males	Urinary incontinence, UTI See text
Ureterocele	Orthotopic or ectopic	None	Reported in females	See text
Bladder hypoplasia or agenesis	Continual dripping of urine; can be associated with ectopic ureter	Various	Females	Urinary incontinence, UTI
Pelvic bladder	Trigone positioned in pelvic cavity, short urethra (in females)	Various	Males and females	Can be associated with urinary incontinence. See text
Bladder exstrophy	Failure of the abdominal wall to close during fetal development results in protrusion of the bladder wall through the ventral abdominal wall. Other viscera such as intestines and genitalia may also be involved.	English bulldog	Females	Urinary incontinence, UTI
Urachus anomalies	Incomplete closure of urachus after birth; various malformations can occur, *e.g.* a diverticulum of the cranial bladder wall, urachal cysts, patent urachus	Various breeds	Males and females	UTI, urinary incontinence. See text
Calculi associated with congenital metabolic defects	Tubular defects in cystine transport giving rise to cystine calculi Altered uric acid metabolism results in inadequate transformation of uric acid to allantoin and the formation of urate calculi Hepatic-vascular defects (portosystemic shunts) cause hepatic dysfunction with a consequent reduction in the conversion of uric acid to allantoin and the formation of urate calculi	Various breeds Dalmatian Larger breeds (intra-hepatic shunts) Toy breeds (extra-hepatic shunts)	Males and females Males	Dysuria, stranguria, pollakiuria, hematuria, UTI
Urethral aplasia or hypoplasia	Incomplete development of the urethra, with the bladder attached to the vagina	None	Females	Urinary incontinence. See text
Urethral-rectal fistula	Fistula formation between the urethra and large intestine	English bulldog	More frequent in males than females	Dysuria, abnormal feces, wet perineum, UTI
Urogenital malformation	Seen especially with pseudo-hermaphroditism, resulting from concurrent development of the organs derived from the Müllerian ducts (uterus, oviduct and part of the vagina) and masculinization of the urogenital sinus	None	Males and females	Dysuria, urinary incontinence, UTI
Epispadia and hypospadia	Epispadia: a congenital defect whereby the distal urethra varies in size and the meatus is positioned too far dorsally Hypospadia: a congenital defect seen mainly in males whereby a malformation of the penis and prepuce results in the urethra being incorrectly positioned ventrally	None Boston terrier	Males and females Males	May be asymptomatic
Urethral prolapse	Severe protrusion of the urethral mucosa	Brachycephalic breeds	Males	Blood on prepuce
Urethral duplication	A defect normally associated with duplication of other organs (rectum, colon, bladder, vagina, penis) or anomalies such as renal hypoplasia or cryptorchidism; usually identified in immature dogs	None	Males and females	Various depending on the type of anomaly: urinary incontinence, UTI
Ectopic urethra	Anomalous positioning of the urethral meatus	English bulldog	Female	Often asymptomatic; possible UTI

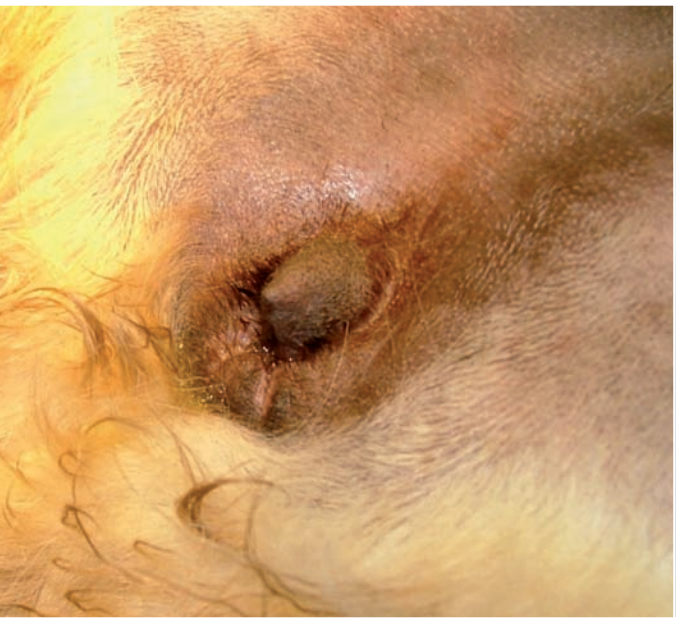


Figure 1. The perivulvar region of a 4-month-old golden retriever female puppy with an ectopic ureter, presented with continual loss of urine.

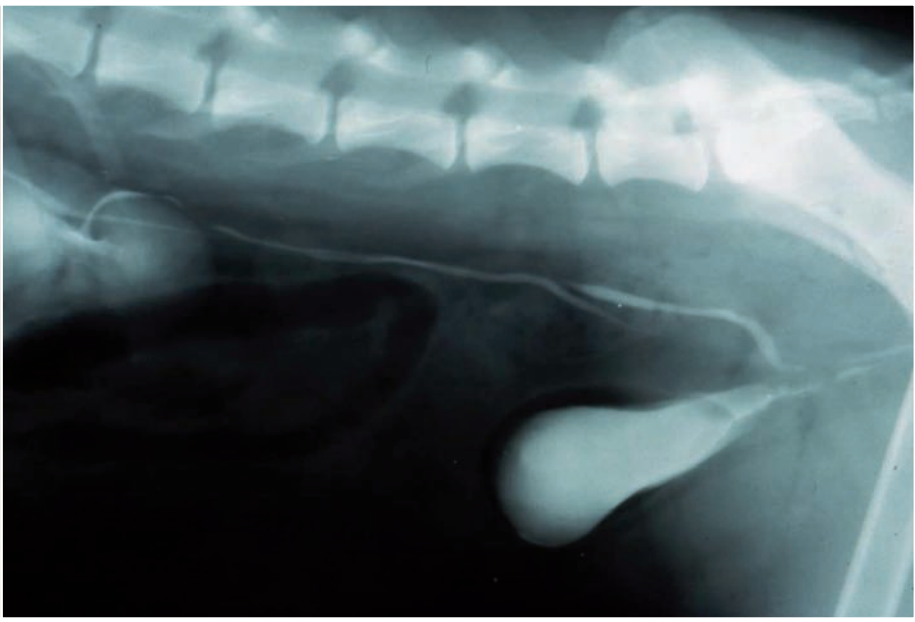
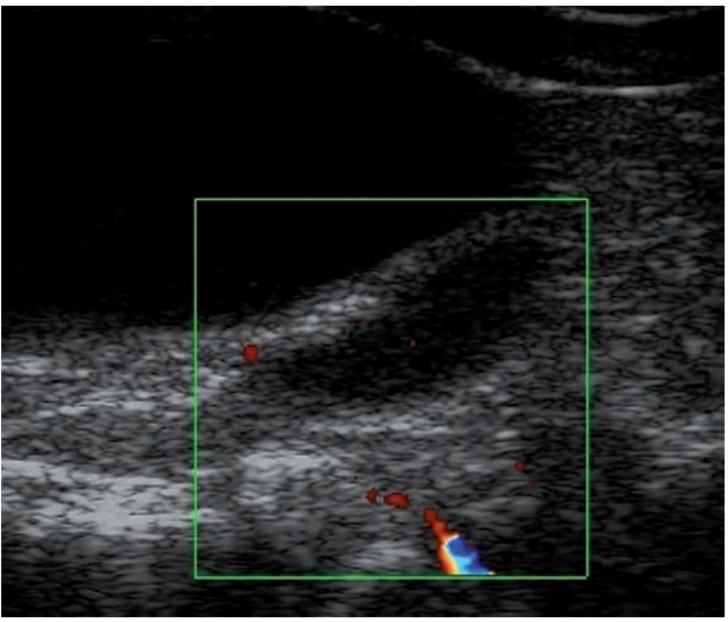


Figure 2. Excretory urography and cystography in a 18-month-old female mixed breed dog with extramural ectopic ureters. Note that the right ureter runs parallel to the urethra for a considerable distance.

are involved in development of the ureters. Due to the close correlation with the mesonephrons, ectopic ureters can be associated with other congenital anatomical anomalies such as renal hypoplasia, ureteroceles, urachal residues and alterations in the vaginal anatomy. In the female, an ectopic ureter can end in the urethra, at the neck of the bladder, in the vagina, or (more rarely) in the uterus. In males, an ectopic ureter normally opens into the urethra (3). An ectopic ureter is defined as being intramural if it is located within the bladder but ends in an anomalous position; sometimes the ureter will enter the bladder at the level of the trigone but continue within the bladder wall before ending distally in the urethral lumen or in the genital tract. An ectopic ureter is defined as being extramural when it runs completely outside the bladder wall before entering the urethra at some point.

The most common clinical presentation is urinary incontinence, which may or may not be associated with urinary tract infection (UTI). Typically urine may be noted dripping at the genitalia. In a female the vulva is persistently wet, with the hair foul-smelling and impregnated with urine ***(Figure 1)*** (This may be differentiated from incontinence post-ovariohysterectomy, when urine is typically voided during or after a period of rest or sleep.).

In males, due to the long urethra, the presence of the prostate, and the resistance of the peri-urethral tissues, symptoms may be less obvious. The diagnosis is confirmed by detecting the anatomical defect by imaging. Traditionally, excretory urography was the method of choice to identify an ectopic ureter and the anomalies often associated with it *(e.g.,* mega-ureter, hydronephrosis) ***(Figure 2)***. Ultrasound scanning can also identify the ectopic nature of the terminal portion of the ureter, making it possible to assess the ureter's exit point in the bladder trigone, which in certain cases can be very close to the start of the urethra. Doppler color imaging can assist in assessing urine peristaltic flow ***(Figure 3)***. One study has shown that excretory urography and ultrasound offer a similar diagnostic sensitivity of around 91% (4) but a volume computed tomography (CT) scan with contrast and cystoscopy currently offers the best diagnostic accuracy. CT imaging allows the trajectory of the ureter and the intra- or extra-mural nature of the defect to be determined accurately ***(Figure 4)***. Cystoscopy can identify the position of the ectopic opening of the ureter, and also allows introduction of a probe through the endoscope channel to identify if there are multiple connections between the ureter, bladder trigone and urethra (5) ***(Figure 5)***. With these patients, it is important to bear in mind that UTI is common and that any infection must be



© Dr. Claudio Brovida

Figure 3. Ultrasound image showing an intramural ectopic ureter extending beyond the bladder trigone.

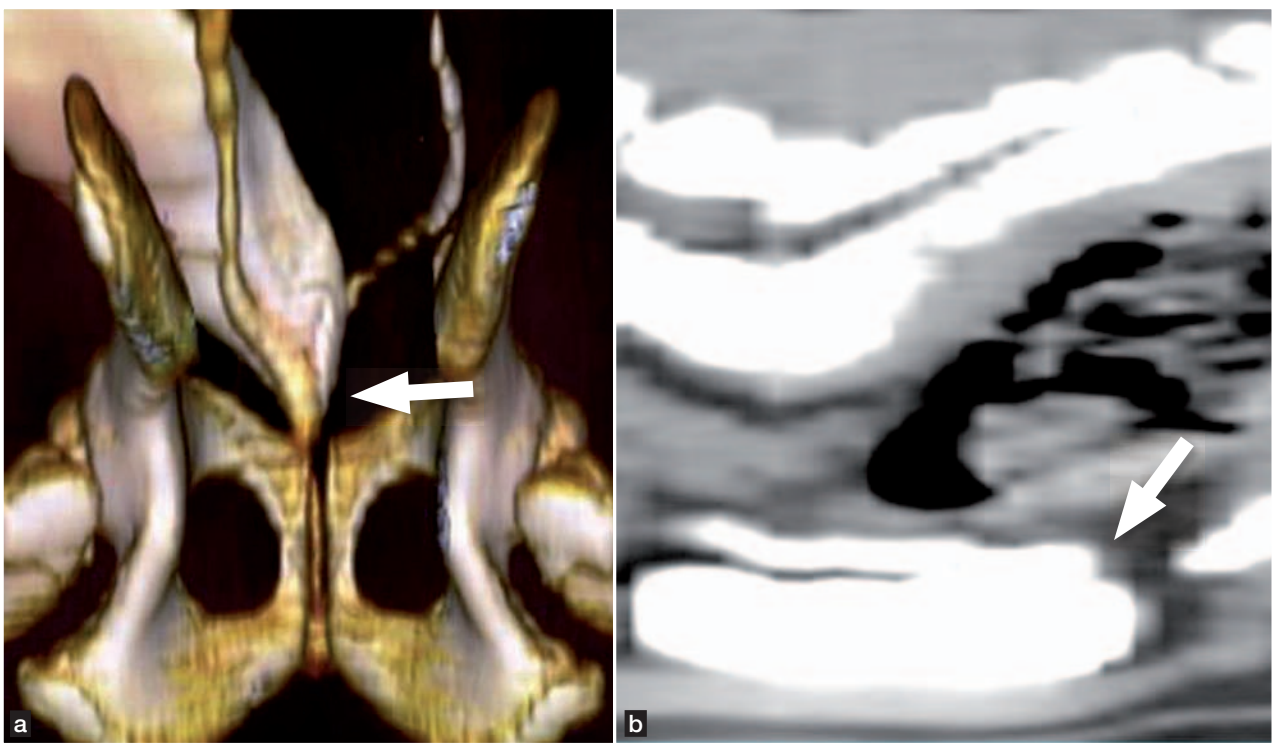
adequately controlled by appropriate antimicrobial treatment before conducting more invasive diagnostic procedures to assess the anatomical defect.

Ectopic ureters can be treated endoscopically or surgically. Intramural ectopic ureters can be ablated using laser therapy with endoscopic guidance. This technique has the double advantage in that it is non-invasive (6) and can be carried out at the same time as diagnosis. Surgical correction of an intramural ectopic ureter is done via cystotomy, exposing the bladder lumen via a midline approach. Extramural ureters that completely bypass the bladder neck are re-implanted in the bladder after the distal portion is dissected free (7). Resolution of incontinence is achieved in about 59% of cases (8) but dogs that continue to show incontinence may also have functional anomalies of the bladder neck and urethra (9).

Ureteroceles

A ureterocele is a cystic dilation of the distal portion of the ureter at the level of the bladder trigone, often protruding inside the bladder itself (10-12). The ureterocele's position can be intravesical (orthotopic), or outside the

Figure 4. CT images of the bladder from the dog in ***Figure 1.*** **(a)** A three-dimensional reconstructed CT image shows the left ectopic ureter running distal to the bladder towards the urethra (arrow), while the right ureter ends correctly at the level of the bladder trigone. **(b)** A longitudinal sagittal CT image reconstruction of the bladder post-contrast shows the course of the ectopic ureter as it runs parallel to the wall of the bladder and beyond it, rather than ending at the trigone (arrow).



© Dr. Claudio Brovida

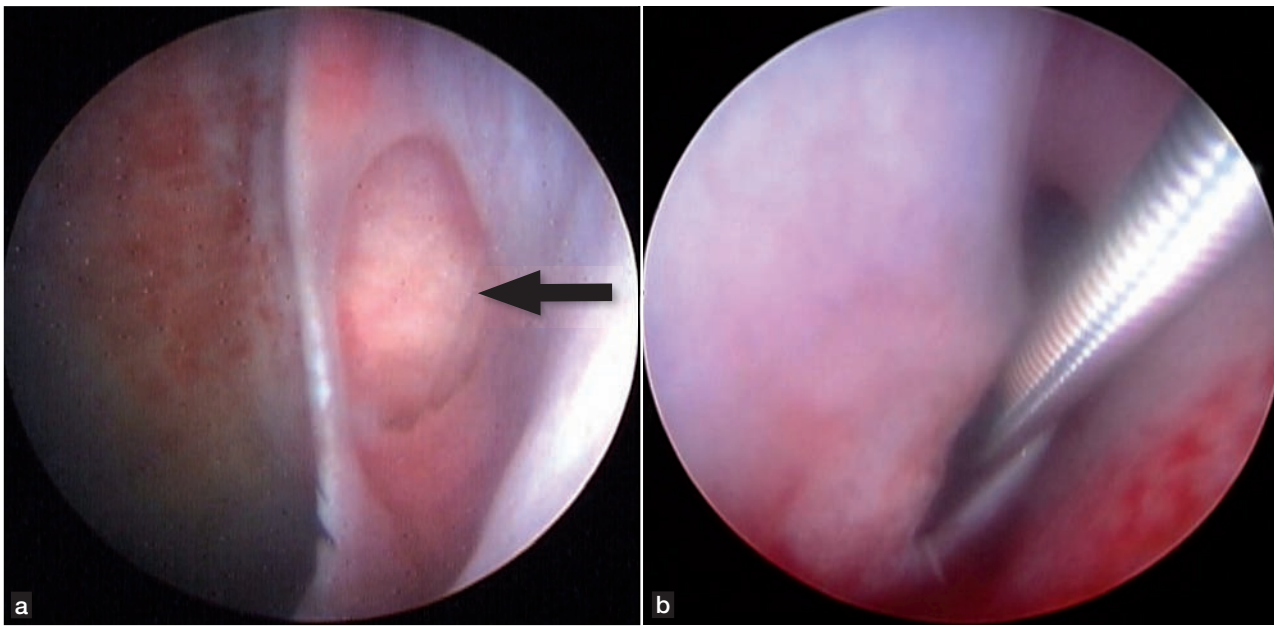


Figure 5. Cystoscopic views of an ectopic ureter; **(a)** the ectopic ureter enters the bladder (arrow) and continues caudally into the urethra. **(b)** A probe inserted by cystoscopy into the ureter's opening in the urethra.

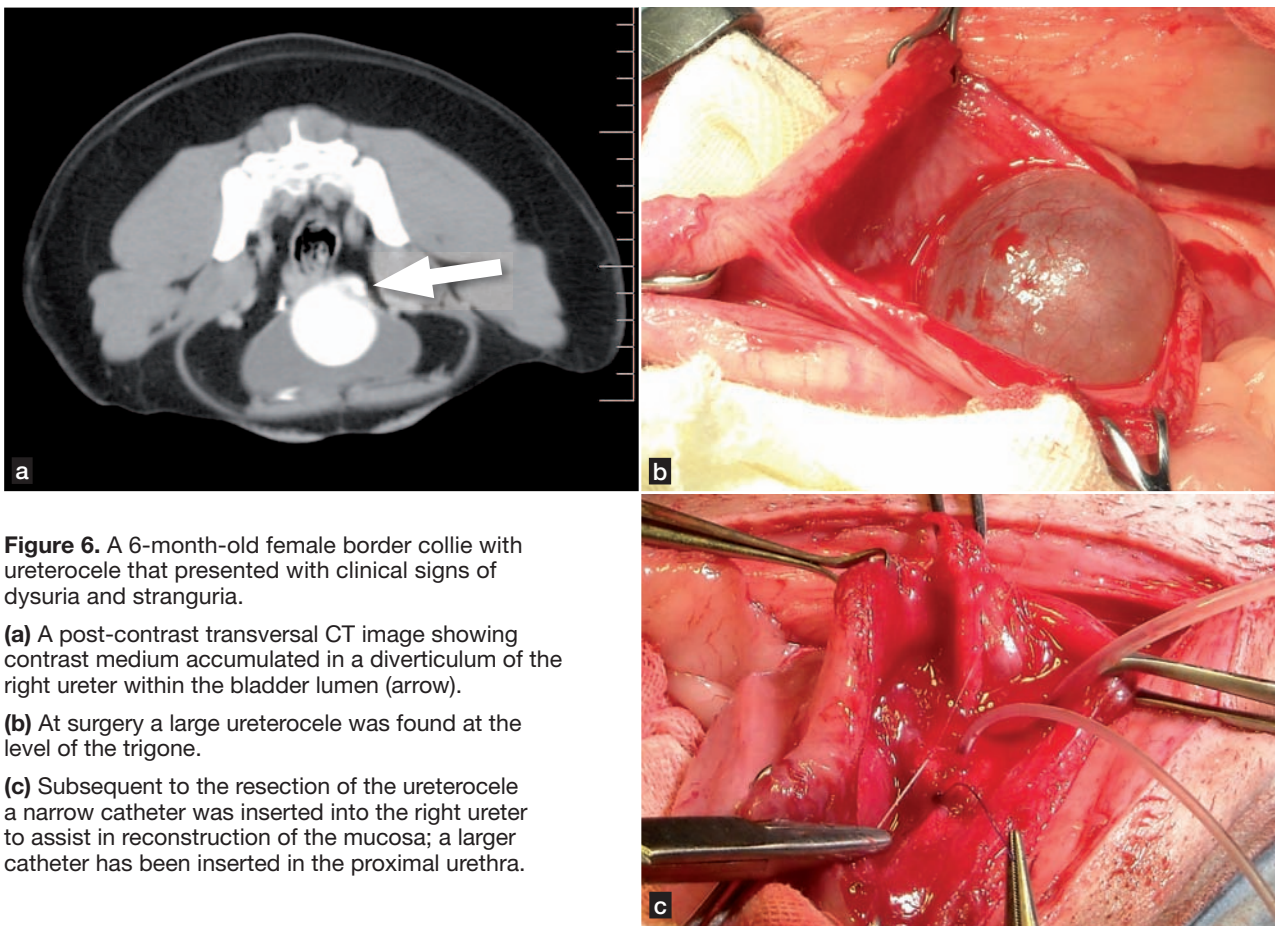


Figure 6. A 6-month-old female border collie with ureterocele that presented with clinical signs of dysuria and stranguria.

(a) A post-contrast transversal CT image showing contrast medium accumulated in a diverticulum of the right ureter within the bladder lumen (arrow).

(b) At surgery a large ureterocele was found at the level of the trigone.

(c) Subsequent to the resection of the ureterocele a narrow catheter was inserted into the right ureter to assist in reconstruction of the mucosa; a larger catheter has been inserted in the proximal urethra.

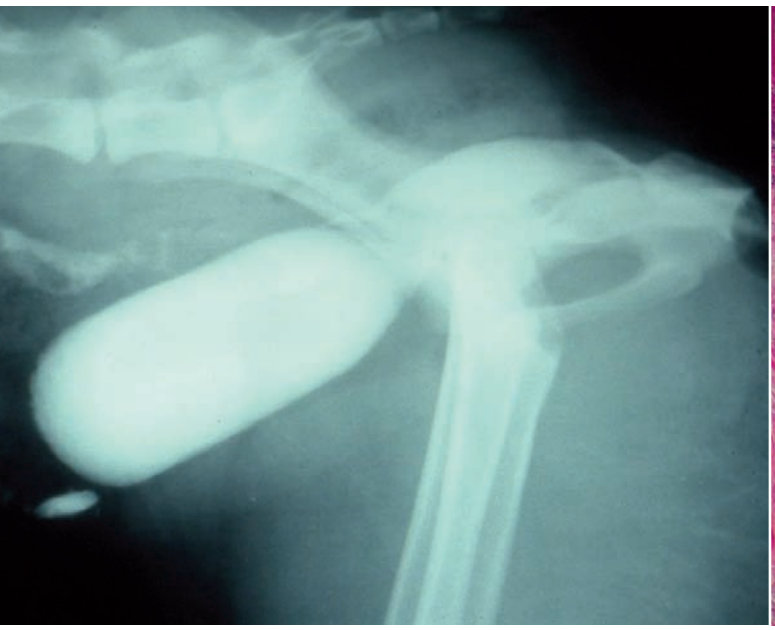
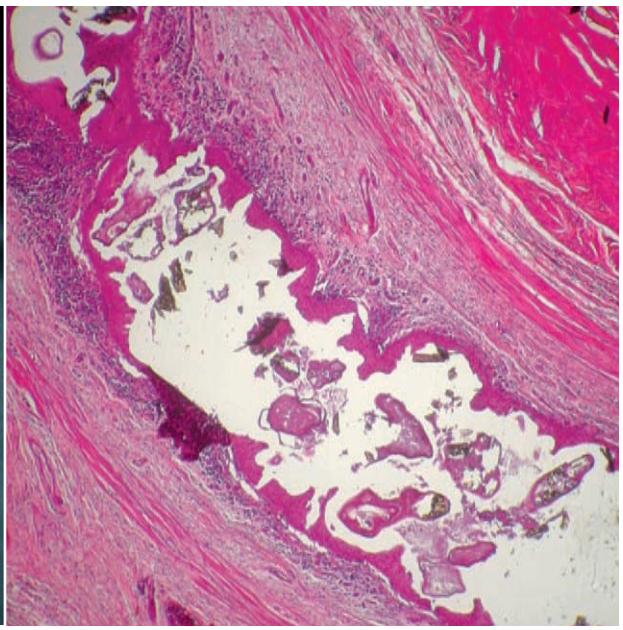


Figure 7. Urachal cysts in a 4-year-old female dog with recurring UTI, diagnosed using retrograde contrast cystography.



© Dr. Claudio Brovida

Figure 8. Histopathological section of a vesico-urachal diverticulum in a 3-year-old female Newfoundland dog that presented with recurring UTI. Surgical removal of the defect during ovarohysterectomy was curative. The diverticulum consists of abundant fibrovascular tissue with multifocal areas of squamous metaplasia and chronic inflammatory cells (lymphocytes, plasma cells and a few macrophages). There is partially mineralized amorphous material within the lumen of the defect.

bladder caudal to the trigone (ectopic). Signs can be completely absent initially but may develop with time, and may vary depending on the exact nature of the defect (*e.g.,* urinary incontinence if there is an ectopic ureter (11,12)). Cyst formation can cause compressions at varying levels of the trigone or proximal urethra, causing urinary retention with dysuria or stranguria. Megaureter and hydronephrosis can also develop as a consequence of persistent compression of the ureteral lumen, and recurring UTI is a common complication.

Ureteroceles can be diagnosed using ultrasound scans (13), excretory urography, CT, or cystoscopy. Treatment consists of initially resolving any infectious complications and subsequently arranging for the surgical elimination of the defect ***(Figure 6)***. When available, laser therapy via cystoscopy can provide an excellent option for treating orthotopic ureteroceles (11-13).

Persistent urachus

During the embryonic phase, urine stored in the bladder is eliminated through the urachal canal which connects the bladder to the umbilicus. After birth, the urachus normally atrophies to a thin fibrous connective tissue remnant attached to the cranial aspect of the bladder, but in some cases the urachal closure is incomplete, giving rise to a variety of anatomical anomalies: i) a residual portion can remain, leading to a vesico-urachal diverticulum, ii) a urachal cyst can form cranial to the bladder if the epithelium continues to secrete fluid or continuity with the bladder lumen persists ***(Figure 7)***, or iii) the urachus can remain open and connect with the umbilicus. Urachal diverticuli can vary in size from extremely small (and possibly invisible macroscopically) to large, easily identified recesses (1). Both diverticuli and cysts can cause urine stagnation, encouraging bacterial infection; the consequent inflammation may allow the cyst or diverticulum to gradually increase in size. Alternatively infected diverticula can regress or disappear totally over time if the UTI is eliminated with antimicrobial therapy. Similarly, the signs will vary depending on the extent of the defect. If the urachus remains patent, urine loss will be noted at the umbilicus; in the case of a very small diverticulum, there may be no signs and the anomaly may be discovered by chance ***(Figure 8)***. The most common finding is associated with the presence of recurrent lower urinary

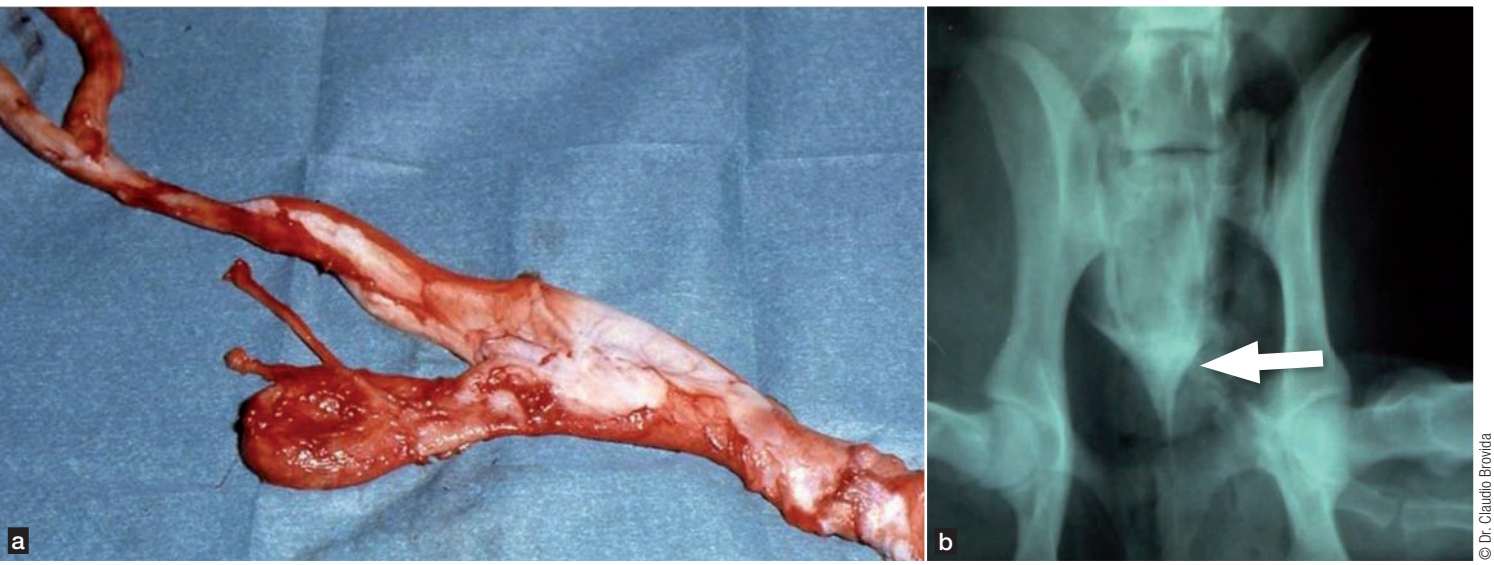


Figure 9. (a) The urogenital tract of a 2-year-old female sheepdog seen at autopsy. The dog was incontinent due to a pelvic bladder and urethral hypoplasia. Note that the bladder is directly connected to the vagina.
(b) Radiograph of the same case using a double contrast technique to outline the defect; the contrast medium does not accumulate in the bladder and passes directly from the ureter into the urethra (arrow).

tract infection secondary to the urachal diverticulum, which causes stagnation of small quantities of urine. In other circumstances a residual urachus may be detected as a result of investigating signs related to other urinary tract anomalies such as bladder calculi.

The diagnosis of vesico-urachal diverticulum can be made via ultrasound scan, contrast cystography and cystoscopy. Where there is a persistent patent urachus with urine loss at the umbilicus, cystography will demonstrate the duct. Treatment is initially directed at eliminating any UTI (14,15) but if the infection persists and imaging techniques confirm the anatomical defect it may be necessary to eliminate the diverticulum surgically by reconstructing the cranial portion of the bladder.

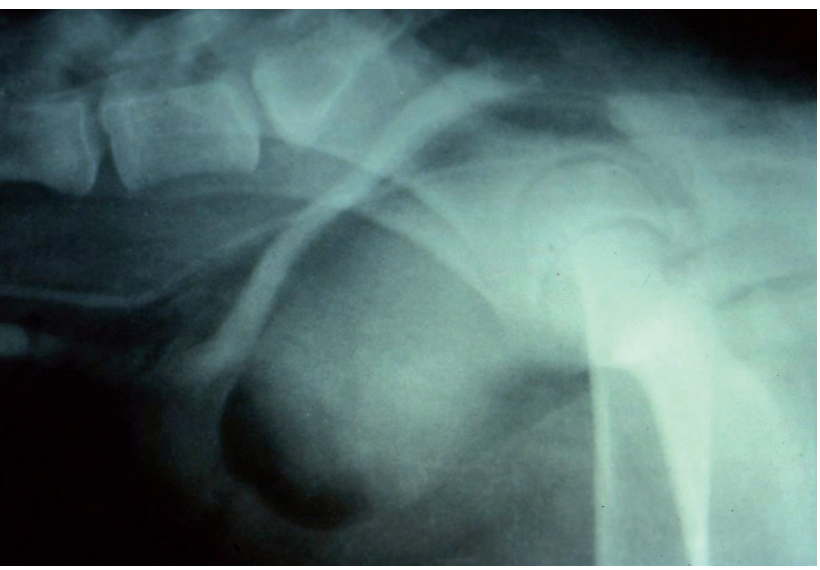


Figure 10. Excretory urography and double contrast cystography used to identify a pelvic bladder and ectopic megaureter.

Pelvic bladder

The term "pelvic bladder" refers to a defect in the positioning of the bladder, whereby the trigone is found to be caudal to the pubis. This defect can be associated with a short urethra or urethral hypoplasia ***(Figure 9)*** but the definition can be controversial and the exact diagnosis of the defect greatly depends on how thoroughly contrast radiological examination (vagino-urethral retrograde cystography) is performed, and it is essential to achieve adequate distension of the bladder during imaging (16). Signs (such as urinary incontinence) may or may not be noted (17) if a pelvic bladder is present. In some cases urinary incontinence which is unresponsive to treatment without other obvious causes (18) may be the primary presenting sign, but concurrent factors such as UTI and/or ectopic ureters can influence the presentation. As mentioned above, the diagnosis is confirmed using contrast radiography ***(Figure 10)***. Urinary incontinence may be controlled with αα-adrenergic agonists, but if pharmacological treatment is unsuccessful, consideration can be given to collagen

injections at the level of the urethra, or achieving abdominal positioning of the bladder via urethropexy or colposuspension (19,20).

Conclusion

When persistent urinary incontinence is diagnosed, or recurrent UTI continues despite antimicrobial treatment, it is important to consider the presence of urogenital defects in the differential diagnosis. The correct diagnosis is based on the detection and localization of the anatomical defect and current diagnostic methods, especially CT and cystoscopy, allow an accurate assessment of such problems. Before performing diagnostic tests it is very important to correctly sterilize the urinary tract if UTI is present, ensuring that any pathogenic bacteria is isolated and the most appropriate and least nephrotoxic antimicrobial medication is chosen. Given that some of the anomalies referred to above can be associated with direct or indirect involvement of the kidneys, it is also essential to exclude the possible presence of renal disease and/or defects using appropriate urine and blood analysis, and imaging as necessary.

References

1. Kruger JM, Osborne CA, Lulich JP. Inherited and congenital disease of the lower urinary tract. In: Osborne CA, Finco DR, eds. *Canine and Feline Nephrology and Urology*. Williams & Wilkins, Baltimore, 1995:681-692.
2. Barges J, Kruger JM. Congenital diseases of the lower urinary tract. In: Bartges J and Polzin D, eds. *Nephrology and Urology of Small Animals*. Wiley-Blackwell, Chichester, 2011:809-817.
3. Osborne CA, Johnston GR, Kruger JM. Ectopic ureters and ureteroceles. In: Osborne CA, Finco DR, eds. *Canine and Feline Nephrology and Urology*. Williams & Wilkins, Baltimore, 1995:608-622.
4. Lamb CR, Gregory SP. Ultrasonographic findings in 14 dogs with ectopic ureter. *Vet Radiol Ultrasound* 1998;39:218-223.
5. Cannizzo KL, McLoughlin MA, Mattoon JS, *et al*. 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.
6. Berent AC, Mayhew P. Cystoscopic-guided laser ablation of ectopic ureters in 12 dogs. *J Vet Intern Med* 2007;21:600(abstract).
7. Stone EA, Mason LK. Surgery of ectopic ureters: types, method of correction, and postoperative results. *J Am Anim Hosp Assoc* 1990;26:81.
8. McLaughlin R, Miller CW. Urinary incontinence after surgical repair of ureteral ectopia in dogs. *Vet Surg* 1991;20:100.
9. Lane IF, Lappin MR, Seim HB. Evaluation of results of preoperative urodynamic measurements in nine dogs with ectopic ureters. *J Am Vet Med Assoc* 1995;206:1348-1357.
10. Lautzenhiser SJ, Bjorling DE. Urinary incontinence in a dog with an ectopic ureterocele. *J Am Anim Hosp Assoc* 2002;38:29-32.
11. McLoughlin MA, Hauptman JG, Spaulding K. Canine ureteroceles: a case report and literature review. *J Am Anim Hosp Assoc* 1989;25:699-706.
12. Stiffler KS, Stevenson MA, Mahaffey MB, *et al*. Intravesical ureterocele with concurrent renal dysfunction in a dog: a case report and proposed classification system. *J Am Anim Hosp Assoc* 2002;38:33-39.
13. Takiguchi M, Yasuda J, Ochiai K, *et al*. Ultrasonographic appearance of orthotopic ureterocele in a dog. *Vet Radiol Ultrasound* 1997;38:398-399.
14. Lulich JP, Osborne CA, Johnston GR. Non-surgical correction of infection-induced struvite uroliths and a vesicourachal diverticulum in an immature dog. *J Small Anim Pract* 1989;30:613-617.
15. Groesslinger K, Tham T, Egerbacher M, *et al*. Prevalence and radiologic and histologic appearance of vesicourachal diverticula in dogs without clinical signs of urinary tract disease. *J Am Vet Med Assoc* 2005;226:383-386.
16. Adams WH, DiBartola SP. Radiographic and clinical features of pelvic bladder in the dog. *J Am Vet Med Assoc* 1983;182:1212-1217.
17. Mahaffey MB, Barsanti JA, Barber DL, *et al*. Pelvic bladder in dogs without urinary incontinence. *J Am Vet Med Assoc* 1984;184:1477-1479.
18. Lane IF, Lappin MR. Urinary incontinence and congenital urogenital anomalies in small animals. In: Bonagura JD, Kirk RW, eds. *Current Veterinary Therapy XII*. Saunders, Philadelphia;1995:1022-1026.
19. White RN. Urethropexy for the management of urethral sphincter mechanism incompetence in the bitch. *J Small Anim Pract* 2001;42:481-486.
20. Holt PE. Long-term evaluation of colposuspension in the treatment of urinary incontinence due to incompetence of the urethral sphincter mechanism in the bitch. *Vet Rec* 1990;127:537-542.
21. Adams LG, Syme HM. Canine ureteral and lower urinary tract diseases. In: Ettinger SJ, Feldman EC, eds. *Textbook of Veterinary Internal Medicine,* 7th Edition. Saunders Elsevier, St. Louis, 2010:2113-2115.

Urates in bladder disease

Cecilia Villaverde, BVSc, PhD, Dipl. ACVN, Dipl. ECVCN
Universitat Autònoma de Barcelona (UAB), Barcelona, Spain

Dr. Villaverde obtained both her veterinary degree (in 2000) and her PhD in animal nutrition (in 2005) at the UAB. She then worked as a post doctoral researcher in feline nutrition at the University of California, Davis (UCD), where she also completed a two-year residency in Small Animal Clinical Nutrition at the Veterinary Medical Teaching Hospital. She achieved board certification in veterinary nutrition by the American College of Veterinary Nutrition and by the European College of Veterinary and Comparative Nutrition in 2010. Currently she is the chief of service of the Servei de Dietètica i Nutrició at the Fundació Hospital Clínic Veterinari, UAB.

Introduction

Urate uroliths ***(Figure 1)*** are metabolic uroliths composed of salts of uric acid, a product of purine metabolism. The most common urate found in canine and feline uroliths is ammonium urate, formed when the urine is supersaturated with uric acid and ammonium ions (1).

KEY POINTS

- **Some canine breeds, most notably the Dalmatian, have a confirmed genetic mutation affecting purine metabolism which predisposes them to urate urolithiasis. Although suspected, a genetic basis has still not been identified in cats.**
- **Liver disease, in particular portovascular anomalies, can also result in urate urolithiasis in dogs and, less commonly, in cats. The pathogenesis of this disease in cats is largely unknown.**
- **Urate bladder stones can potentially be dissolved in dogs using a combination of a low-purine diet, urine dilution, urine alkalinization and xanthine oxidase inhibitors. A similar protocol has not been established for cats, and surgery is the treatment of choice in this species.**
- **Diet is considered important in preventing recurrence. A thorough diet history is important to facilitate recommendations for the best diet in each case. These diets should be low in purine, alkalinizing in nature and (if possible) capable of promoting a dilute urine.**

Urate-containing uroliths are usually reported as the third most common urolith type in dogs and cats, after struvite and calcium oxalate. The percentage of these uroliths submitted to analysis varies depending on the laboratory and the geographical location, and ranges from 3.1-25% of submissions in dogs (2-4) and from 3.9-10% in cats (2,5,6) but the disease incidence is thought to have remained static for the last two decades. Recurrence rates have been reported to range between 4-13% in cats (7,8) whilst one study reported a recurrence rate of 22% in Dalmatians (9). Recurrence can be due to persistence of underlying risk factors, lack of owner compliance or incomplete removal of the stones at the time of surgery (8).

Some canine breeds, such as the Dalmatian ***(Figure 2)***, have been shown to have a genetic predisposition to this disease (1). Dogs can also develop urate urolithiasis as a consequence of liver disease, particularly portovascular anomalies (10).

In cats, the cause of urate uroliths is largely unknown. A genetic predisposition has not yet been proven, but some breeds are over-represented (2), which suggests this is a possibility. Felines can also develop urate stones secondary to portovascular anomalies.

Purine metabolism

Purines in the body originate from endogenous nucleotide metabolism and can also come from the diet. The end product of purine catabolism in humans and primates is uric acid, obtained by the action of the enzyme xanthine oxidase on hypoxanthine and xanthine. In most mammals, however, uric acid is further metabolized by hepatic uricase to allantoin, which is then excreted through the urine ***(Figure 3)***. Thus although some uric

acid is excreted, allantoin is the main end product of purine metabolism in dogs and cats (11). Allantoin is more soluble in canine and feline urine than uric acid; this means that as the percentage of uric acid excreted in the urine increases, so does the risk of urate urolithiasis.

Risk factors

Breed

Dalmatians are genetically predisposed to this disease. It has been known for some time that the main end product of purine metabolism in this breed is uric acid rather than allantoin (1) and it has been shown recently that Dalmatians are homozygous for a mutation that results in a defect of the hepatic and renal uric acid transporter (SLC2A9) (12). The defective transporter results in i) a lower conversion of uric acid to allantoin and ii) a lower reabsorption of uric acid by the proximal renal tubules. This in turn results in hyperuricemia and hyperuricosuria, predisposing this breed to urine super-saturation with uric acid. Dalmatians excrete 400-600 mg/ uric acid per day, compared to 10-60 mg per day in other breeds (13).

Most of the canine urate-containing uroliths submitted for analysis are from Dalmatians (2) and the prevalence of clinical disease in male Dalmatians is estimated to be high. Female Dalmatians rarely manifest clinical urate urolithiasis, although they are also homozygous for the mutation. It is unclear why there is a gender bias, although possible explanations include anatomical, genetic or urine composition differences (11).

The same mutation has also been shown to exist in other breeds prone to urate urolithiasis, such as the English bulldog and black Russian terrier (14). A genetic test is available in some countries which can help identify heterozygous (non-Dalmatian) carriers before breeding.

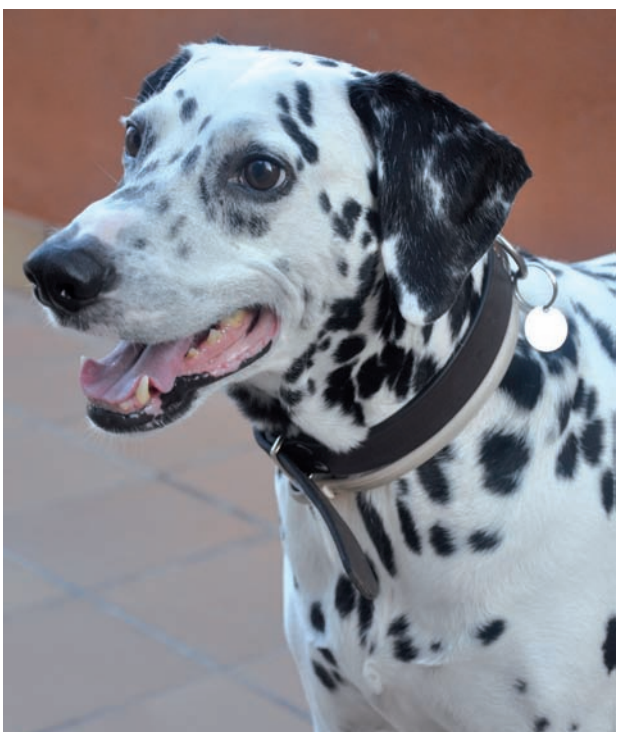
The Yorkshire terrier is also frequently associated with urate urinary stones, and this is probably because they are predisposed to portosystemic shunts rather than to a specific alteration of their purine metabolism.

In cats, some studies have found that Siamese cats are at risk for urate urolithiasis (5,6). One study also found an association between this disease and Egyptian mau and Birman cats (6). Some breeds such as the Persian are under-represented (15). More research is needed in order to clarify further if there is a genetic predisposition to urate urolithiasis in felines.

© Dr. Andrew Moore, CVUC, Guelph, Ontario, Canada

Figure 1. Urate stones can vary in shape, size and appearance.

Figure 2. Male Dalmatian dog with a history of urate urolithiasis.


© Dr. Cecilia Villaverde

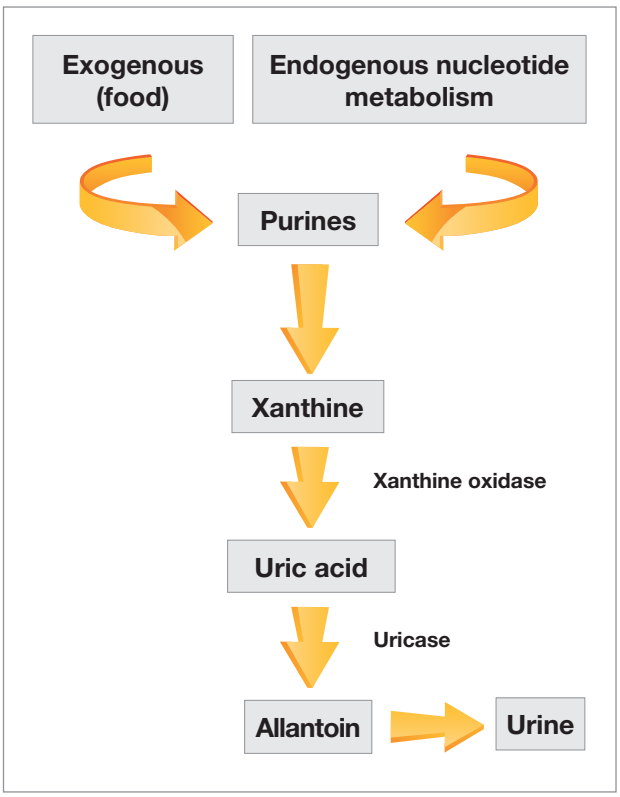


Figure 3. A schematic diagram showing purine metabolism.

Liver disease

Severe liver dysfunction, especially portosystemic shunts, can predispose both dogs and cats to urate uroliths (1). Since the conversion of uric acid to allantoin takes place in the liver, affected animals have higher concentrations of uric acid in the blood, which may result in higher uric acid urine excretion.

Liver dysfunction is also associated with hyperammonemia, due to a lower hepatic conversion of ammonia to urea. This will result in a higher urinary excretion of ammonia, which can then bind with uric acid to form uroliths.

Liver disease as a cause of urate urolithiasis in cats is considered rare. One study evaluated 143 cases of feline urolithiasis (from both primary and secondary care clinics) and found evidence of possible liver dysfunction in only 4.9% of cases, with a portosystemic shunt confirmed in just 1.2% of cases (7). Even though not all cats in the study were investigated for liver disease, these results suggest that portosystemic shunts are not a common cause of feline urate urolithiasis.

Other factors

In dogs, breed and liver disease are the main risk factors for this disease. Males have a higher incidence if the disease is not associated with a portosystemic shunt. Other suggested risk factors are hyperuricemia, hyperammonemia, hyperuricosuria, hyperammonuria and aciduria (11).

In cats, neuter status and age were identified as risk factors in one study; neutered cats and/or animals between 4-7 years of age were at greater risk of developing urate urolithiasis (15). Cats with urate urolithiasis secondary to liver disease were significantly younger than cats where liver disease was not identified (7). Gender is not considered to be a risk factor, although a study found that males had a slightly higher risk (6). One report suggested that hyperuricosuria is also a risk factor in cats (16).

In humans, the prevalence of uric acid and calcium oxalate urolithiasis increases with body size (17). Data in this species suggests obesity is associated with a decreased excretion of urinary citrate (a stone inhibitor) and is also inversely correlated to urinary pH (18). A link between obesity and urate urolithiasis in dogs and cats has not been described.

Dietary management of urate urolithiasis

Dissolution

Urate stones not associated with portovascular anomalies can potentially be dissolved in dogs ***(Figure 4)***. In one study, the dissolution protocol resulted in total dissolution in a third of the dogs, reduction in size and number of uroliths in another third, and no success in the remainder (1). A dissolution protocol typically includes a low-protein/low-purine diet, urine alkalinizing agents (such as potassium citrate), and xanthine oxidase inhibitors such as allopurinol, at the dose of 15 mg/kg PO q 12H. Alkalinizing agents might not be necessary if the diet results in a urine pH >7. Uroliths should reduce in size and number by half every 4 weeks. Alkalinization is important because it increases the solubility of the precursors (19).

There are no dissolution protocols for patients with portosystemic shunts. In cats, there are no protocols established for dissolution, and the safety of xanthine oxidase inhibitors has not been established, so surgery is therefore the treatment of choice in this species.

Prevention

In patients with portosystemic shunts, recurrence can

be avoided by correcting the vascular defect. In cases where the anomaly cannot be surgically repaired, or if the urate stones are due to another cause, preventative measures are necessary. Those include promoting a dilute urine, alkalinizing the urine, and providing a low-purine diet, which requires careful selection of diets plus medication as necessary.

Diet characteristics

Moisture content

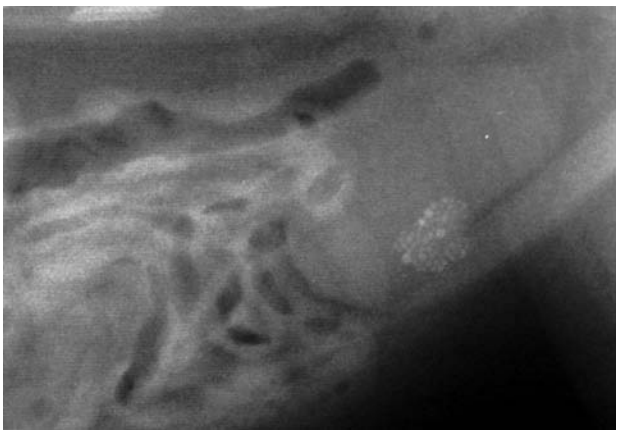
Canned foods are preferable (both for dissolution and prevention) in order to promote a more dilute urine. Sometimes additional water needs to be added to the canned food to achieve the required urine specific gravity (USG) (< 1.020 in dogs and < 1.025-1.030 in cats). The USG can also be decreased by using a low-protein diet (low enough to result in renal medullary washout), by using salt supplementation to promote diuresis (using salt as a diuretic is not recommended in patients with liver disease as they are prone to portal hypertension), and by adding water to the kibble (in a proportion of at least 2 volumes of water to 1 volume of food).

Protein content and type

Traditionally, low-protein diets (8-10% metabolizable energy diets in dogs, 22-27% metabolizable energy in cats) have been recommended in these cases for prevention, although there is now the possibility to use diets higher in protein which are still low in purines. A low-protein diet has several benefits:

- Protein sources usually contain purine, so a low-protein diet is also low in purines.
- A very low-protein diet can promote dilute urine by medullary washout.
- Low-protein diets tend to be alkalinizing (this needs to be confirmed by the manufacturer due to other acidifying ingredients).

The potential pitfalls of this approach are low palatability and the risk of protein and amino acid deficiencies. Some commercial diets for the management of urate stones provide a level of protein below what is legally recommended for adult maintenance, but they still provide the essential amino acids in amounts above the minimum requirements to prevent protein deficiencies. However, their safety margin is lower and the amount of protein provided by these diets could be marginal in some dogs with low energy requirements. There were a few reported cases of dilated cardiomyopathy in Dalmatians (20) when fed a low-protein, urate preventing diet, which were thought to be due to taurine deficiency. Since then, commercial low-protein canine diets,



© Dr. William Widmer

Figure 4. Urate calculi are generally small and may or may not have enough calcium to be visualized radiographically. Some urate stones not associated with portovascular anomalies can be dissolved in dogs.

including the ones for urate prevention, are always supplemented with sulfur amino acids, taurine and L-carnitine.

Protein type can also be important. Some protein sources are lower in purines than others ***(Table 1)*** and so when vegetables, dairy products or eggs are used as protein sources this can result in diets low in purines but moderate in protein. This may be beneficial in patients where a low-protein diet results in loss of muscle mass.

In one study (21), 12 healthy Dalmatians were fed either a commercial over-the counter diet, a commercial low-protein diet formulated to prevent urate urolithiasis (8% protein on an energy basis), or a low-purine experimental diet (16% protein on an energy basis). Both the experimental low-purine and the commercial low-protein diets

Table 1. Purine content of common ingredients (17).

Purine content	Animal products	Vegetable products
Very high	Shellfish, some fish, offal	
Moderately high	Meat (skeletal muscle), some fish	Legumes, spinach, asparagus
Low	Dairy, egg, fats	Bread, oils, grains, fruits, most vegetables

decreased the concentration of uric acid in plasma, and no differences were found in urinary pH and urinary uric acid between the two diets. This study only took a spot urine sample, however, so it is hard to draw conclusions. It was also noted that although the purine content of the experimental diet was low, the actual purine content of the other diets was not measured.

One commercially available diet* suitable for adult maintenance has low-purine ingredients (vegetable protein and egg) and has a protein content of 18% (on an energy basis), and is currently being evaluated in stone-forming Dalmatians. Preliminary results (22) have shown that 6 dogs fed this diet for 2 months (previously fed a lower-protein diet) have maintained a low USG and the same 24-hour urinary excretion of uric acid and allantoin in the urine and remained free of cystoliths, although urinary pH was decreased.

Taken together, these results suggest that both strategies (low-protein/low-purine diets and moderate protein/low purine) are beneficial in preventing urate urolithiasis in dogs, although more research testing these diets in stone-forming animals is required.

*Royal Canin Veterinary Diet Urinary U/C canine dry

Cats have high protein requirements so protein can only be restricted up to a point. The current recommendation is to feed a diet lower in protein than the diet fed at the time of diagnosis; typical moderate protein diets are renal or liver therapeutic formulations. There are no vegetarian diets for cats, but commercial soy-based diets - such as some of the hydrolyzed protein diets - could be used, since soy is a low-purine protein source. Unfortunately there are no data on the efficacy of any of these approaches at this time.

Monitoring

Monitoring every 3-6 months is recommended in cats and dogs with urate urolithiasis. Besides an updated medical history (including diet history) and physical examination, monitoring should include urinalysis and imaging. The goal is to achieve a lower USG (1), an alkaline urine pH, and an absence of urate crystals when the sediment is examined. Imaging should take into account the fact that urate stones are often radiolucent, so either double-contrast cystography or ultrasound should be performed to ensure that the urinary tract is free of uroliths.

References

1. Bartges JW, Kirk CA. Nutritional management of lower urinary tract disease. In: Fascetti AJ, Delaney SJ, eds. *Applied Veterinary Clinical Nutrition*. 1st ed. Chichester: Wiley-Blackwell, 2012:269-288.
2. Houston DM, Moore AEP. Canine and feline urolithiasis: examination of over 50 000 urolith submissions to the Canada Veterinary Urolith Centre from 1998 to 2008. *Can Vet J* 2009;50:1263-1268.
3. Low WW, Uhl JM, Kass PH, *et al*. Evaluation of trends in urolith composition and characteristics of dogs with urolithiasis: 25,499 cases (1985-2006). *J Am Vet Med Assoc* 2010;236:193-200.
4. Roe K, Pratt A, Lulich JP, *et al*. Analysis of 14,008 uroliths from dogs in the UK over a 10-year period. *J Small Anim Pract* 2012;53:634-640.
5. 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;231:570-576.
6. Appel SL, Houston DM, Moore AEP, *et al*. Feline urate urolithiasis. *Can Vet J* 2010;51:493-496.
7. Dear JD, Shiraki R, Ruby AL, *et al*. Feline urate urolithiasis: a retrospective study of 159 cases. *J Feline Med Surg* 2011;13:725-732.
8. Albasan H, Osborne CA, Lulich JP, *et al*. Rate and frequency of recurrence of uroliths after an initial ammonium urate, calcium oxalate, or struvite urolith in cats. *J Am Vet Med Assoc* 2009; 235:1450-1455.
9. Case LC, Ling GV, Ruby AL, *et al*. Urolithiasis in Dalmatians: 275 cases (1981-1990). *J Am Vet Med Assoc* 1993;203:96-100.
10. Marretta SM, Pask AJ, Greene RW, *et al*. Urinary calculi associated with portosystemic shunts in six dogs. *J Am Vet Med Assoc* 1981;178:133-137.
11. McCue J, Langston C, Palma D, *et al*. Urate urolithiasis. *Compend Contin Educ Vet* 2009;31:468-475.
12. Bannasch D, Safra N, Young A, *et al*. Mutations in the SLC2A9 gene cause hyperuricosuria and hyperuricemia in the dog. *PLoS Genet* 2008;4: e1000246.
13. Westropp JL. Current trends in canine urolithiasis (including management). In *Proceedings*. British Small Animal Veterinary Congress 2010;352.
14. Karmi N, Safra N, Young A, *et al*. Validation of a urine test and characterization of the putative genetic mutation for hyperuricosuria in Bulldogs and Black Russian Terriers. *Am J Vet Res* 2010;71:909-914.
15. Albasan H, Osborne CA, Lulich JP, *et al*. Risk factors for urate uroliths in cats. *J Am Vet Med Assoc* 2012;240:842-847.
16. Rivara CM, Shepard S, Johnson CR, *et al*. Hyperuricosuria without alterations in liver function is a risk factor for feline urate uroliths. *J Vet Intern Med* 2011;25:719(abstract).
17. Najeeb Q, Masood I, Bhaskar N, *et al*. Effect of BMI and urinary pH on urolithiasis and its composition. *Saudi J Kidney Dis Transpl* 2013;24:60-66.
18. Larsen JA, Westropp JL. Update on urate urolithiasis. In *Proceedings*. American College of Veterinary Internal Medicine Forum 2013.
19. Ngo TC, Assimos DG. Uric acid nephrolithiasis: recent progress and future directions. *Rev Urol* 2007;9:17-27.
20. Freeman LM, Michel KE, Brown DJ, *et al*. Idiopathic dilated cardiomyopathy in Dalmatians: nine cases (1990-1995). *J Am Vet Med Assoc* 1996;209:1592-1596.
21. Bijster S, Nickel RF, Beynen AC. Comparison of the efficacy of two anti-uric acid diets in Dalmatian dogs. *Acta Vet Hung* 2001;49:295-300.
22. Westropp JL, Larsen JA, Quéau Y, *et al*. Evaluation of urate urolithiasis recurrence and urinary uric acid and allantoin excretion in dogs consuming Royal Canin Veterinary Diet® Urinary UC. In Proceedings. 22nd European College of Veterinary Internal Medicine – Companion Animal Congress 2012.

HOW I APPROACH...

Feline idiopathic cystitis

Pieter Defauw, MVetMed
Faculty of Veterinary Medicine, Ghent University, Belgium

Pieter Defauw graduated from the University of Ghent, Belgium, in 2008 and remained there to complete a one-year small animal rotating internship. He then followed a residency in small animal internal medicine (ECVIM-CA) at the same faculty, completing it in 2013. His main research interests include feline idiopathic cystitis and the use of urinary markers for the detection of renal dysfunction.

Introduction

Feline lower urinary tract disease (FLUTD) is not a single disease process, but rather a term previously used commonly to describe a group of different diseases involving the feline urinary bladder and urethra. All these diseases lead to the same clinical signs, such as dysuria, stranguria, hematuria, pollakiuria, periuria (urinating in inappropriate places – *e.g.,* outside the litter box), and sometimes urethral obstructions. Occasionally only one of these signs is noted, but affected cats usually present with a variable combination of them.

KEY POINTS

- **Feline idiopathic cystitis (FIC) is the single most common cause of both non-obstructive and obstructive signs related to the lower urinary tract in cats.**
- **Cats with urethral plugs in which no underlying disease process (such as urolithiasis) can be identified are likely to have FIC and need to be treated as such.**
- **Abdominal radiography is the most important diagnostic test in cats with obstructive lower urinary tract syndrome.**
- **Increasing water intake and improving the cat's environment are crucial in the long-term management of FIC.**

Etiology

About two-thirds of all cats presented with lower urinary tract signs (LUTS) will have feline idiopathic cystitis (FIC). FIC is diagnosed by exclusion of other diseases (mainly urolithiasis and urinary tract infection (UTI)) that lead to LUTS, as shown in ***Figure 1*** (1-6). Studies conducted at referral practices suggest bacterial cystitis is rare (1-3%) (1-3) but in general practice bacterial cystitis seems to be a more common presentation – one recent study quoted 12% of all cases presented with LUTS had bacterial cystitis (6). Despite this difference, bacterial infections are clearly less common than FIC and urolithiasis, although important exceptions to this general rule are cats with concurrent illness (such as diabetes mellitus or chronic kidney disease) as this can predispose them to bacterial cystitis. Because of the higher prevalence of concurrent disease in older cats, UTI are most commonly diagnosed in cats > 10 years of age. A history of recent urethral catheterization also makes the presence of iatrogenic-induced UTI much more likely. Uncommonly, other causes (such as urinary bladder neoplasia, trauma and anatomic anomalies) are diagnosed. Anecdotally, clinically relevant cystitis caused by the parasite *Pearsonema (Capillaria) plica* has also been reported (7).

The first differential for cats presented in an emergency situation with a urethral obstruction is also FIC ***(Figure 2)*** (1,5). However, it is very important to search for the second most common cause of obstructions, namely urethroliths, because of the significant treatment differences between the two conditions. Urethral plugs are commonly reported as a major stand-alone cause of obstruction (1,2,6), but when uroliths are not present most obstructive cases diagnosed with urethral plugs are likely to have FIC as an underlying disorder, because

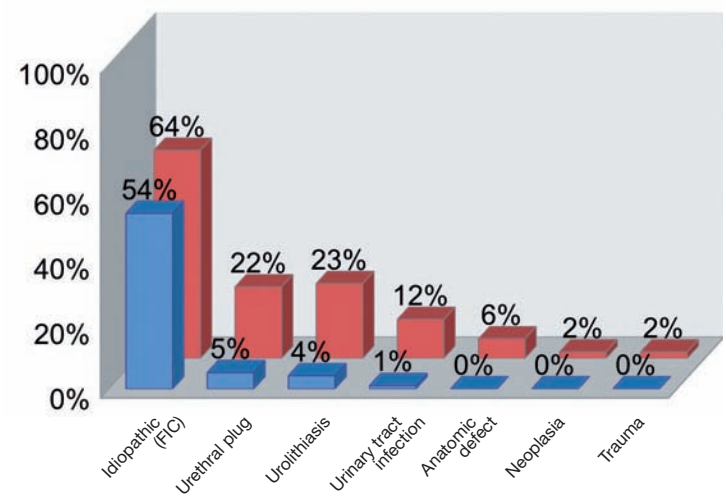


Figure 1. Causes of lower urinary tract signs (both non-obstructive and obstructive) in cats; the figures show the reported minimum and maximum occurrences between different studies (1-6).

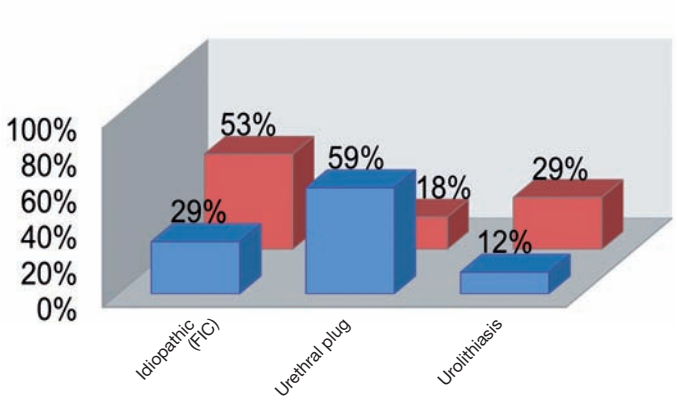


Figure 2. Causes of urethral obstructions in cats as reported in two studies (references 1 (blue) and 5 (red)).

inflammation of the urinary bladder from any cause can theoretically lead to urethral plug formation. By exclusion of other inflammatory conditions, FIC is diagnosed, and by implication treatment for FIC should be applied for all cats with urethral plugs whenever an underlying cause, such as urolithiasis or UTI, is not identified. It is also important to appreciate that one can therefore say that approximately ¾ of all cats with LUTS can be said to have FIC when these cases are included, and that the true proportion of cats that obstruct due to plugs is probably underestimated, because most plugs are flushed back into the urinary bladder during catheterization without visual confirmation of their presence.

Pathophysiology of FIC

Without going into detail, a basic knowledge of the pathophysiology of FIC is necessary as this has management implications. FIC mainly manifests clinically as a disease of the urethra and urinary bladder, but it is important to realize that affected cats seem to have anomalies at many different levels. Although the primary cause is still unknown and many factors are still unclear, several studies have identified anomalies at the level of the urinary bladder, sympathetic nervous system, and cortical adrenal function. It is suggested that an overactivation and/or inadequate suppression of the sympathetic nervous system, together with a lack of cortisol production as a stress response, causes a neurogenic inflammation within the bladder and is responsible for a chronic state of stress in cats with FIC (8,9).

Attempts to decrease the sympathetic overactivation by environmental enrichment and stress reduction have been shown to be effective in the long-term control of FIC (10).

Diagnosis of FIC

A detailed individual behavioral and environmental history should be obtained for all cats with LUTS. Identified risk factors for FIC are shown in ***Table 1*** (11,12). Clients need to be questioned proactively about the presence of potential stressful situations in the cat's environment; specific examples may need to be suggested, as owners will often not recognize these factors as stressful circumstances. Although sometimes supportive for a diagnosis of FIC (when the owner clearly links recurring bouts of LUTS to a specific incident), identifying risk factors and stressful situations for every individual cat is very important for long-term management of FIC, as discussed below.

When presented with a cat showing LUTS, a diagnostic work-up for urolithiasis and UTI needs to be considered before making a presumptive diagnosis of FIC. In the case of a non-obstructive first episode of short duration, a minimal work-up may be appropriate, but an initial more aggressive diagnostic work-up, including medical imaging, should be considered for any male cat with stranguria because of the potential life-threatening complications of a urethral obstruction. Medical imaging is also strongly advised in obstructive, recurrent and/or long lasting episodes. The most important imaging modality

without doubt is plain abdominal radiography to evaluate for the presence of uroliths, and the importance of assessing the entire length of the urethra cannot be overemphasized; since most uroliths in cats are radiopaque, contrast techniques are rarely necessary. Abdominal ultrasound will not detect penile urethral stones, leading to an incorrect diagnosis of FIC.

In many cases, urinalysis (including culture with sampling, preferably by cystocentesis), and abdominal radiography is sufficient for a clinical diagnosis of FIC (*i.e.*, diagnosis by exclusion). Hematuria and proteinuria are common but nonspecific findings in cats with FIC; crystalluria and mild pyuria may also be present. Abdominal ultrasonography is the next diagnostic step and is mainly indicated in cats with a previous diagnosis of FIC unresponsive to treatment, in older cats, or in atypical case presentations - for example, when only periuria is present, it is necessary to differentiate between FIC and a behavioral problem, and this can sometimes be difficult (3). Advanced medical imaging (abdominal ultrasound, contrast cystography, and cystoscopy) are particularly useful in these cases. The presence of signs indicative of systemic disease may also warrant other appropriate investigations.

Treatment of FIC

The recommended standard therapy for cats diagnosed with FIC consists of gradual environmental enrichment and stress reduction, along with increased water intake (13). In the majority of cases implementation of these measures will be sufficient to control FIC long term. Any alteration should not be made suddenly, because drastic changes may elicit new episodes of FIC by themselves.

Multimodal environmental modification

A prospective observational study showed a reduction in LUTS after institution of multimodal environmental modification (MEMO) (10). By reducing stimulation of the overactive sympathetic nervous system, MEMO significantly reduced expression of LUTS. These modifications have been described in detail elsewhere (8) but a major element to consider is the reduction of inter-cat conflict by providing sufficient "resources" for every cat. This means that the traditional rule of "x + 1" (where x is the number of cats in the household), which is often applied to litter boxes (*i.e.,* 1 litter box per cat, plus 1 additional litter box) should be extended to every resource (*e.g.*, sleeping places, food bowls, water bowls), along with considering different and appropriate locations for these resources. Having access to a private place to eat and sleep is important for many of these cats. Stimulating natural predatory behavior can be encouraged with certain toys and also helps to improve interactions with the owner. Wherever possible, providing physical structures for interactions (*e.g.,* climbing, hiding, sleeping, scratching) and/or allowing outdoor access for indoor cats may be a way to reduce stress.

Water management

Studies and clinical experience suggest that decreasing urine specific gravity (USG) by switching to a canned diet improves long-term FIC control (13); this may be because a lower urine concentration could be less irritating for a chronically inflamed bladder wall. Increasing water intake is most easily accomplished by gradually switching to a canned diet, and whilst moving from dry to canned food can be difficult with some cats thorough attempts should always be made. Other options to improve water intake include using various shapes of bowl (or using water fountains) and trying different water types (bottled or tap water).

These preferences are specific to individual cats and can be tested on a "trial and error" basis. An important mechanism employed in several struvite preventative diets is to increase diuresis, and switching to such diets can be considered as an additional way to decrease USG. Urethral obstructions in cats diagnosed with FIC

Table 1. Risk factors in FIC (11,12).

Long hair
Obesity
Low water intake
Low activity level
Less access to outside
Using a litter box
Less hunting behavior
Living in conflict with another cat from the same household
Being less likely to spit at other cats in the neighborhood
Being more fearful and nervous than other cats from the same household
Hiding from unknown visitors in the house
House move

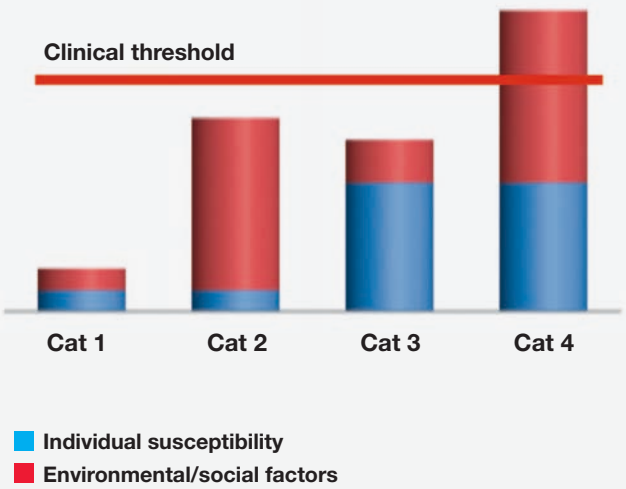


Figure 3. Clinical disease expression of FIC.

A combination of both a susceptible cat and deficient environmental factors is necessary before clinical episodes of FIC occur (*i.e.,* the summation of the factors must be above the clinical threshold). In this illustration, only **cat 4** shows clinical episodes of FIC, because this cat has a high individual susceptibility and lives in a deficient environment. **Cat 3** is as susceptible as **cat 4** for clinical episodes, but never shows signs of FIC because there are only minor environmental deficiencies present. **Cat 2** lives in a highly deficient environment but never shows signs of FIC because of a very low individual susceptibility.

The main goal of long-term therapy is to improve social and environmental factors to reduce and maintain this combination below the clinical threshold.

are also more likely in cats with struvite crystalluria (12). Knowing that urethral plugs are often partly composed of struvite crystals, prevention of new plug formation by reducing crystal formation through dietary modifications might be appropriate in these cases. Interpretation of these findings is however complicated by the presence of urinary crystals in normal cats as well.

Disease expression

Stressful situations and deficient environmental factors are present in most modern households, yet only a minority of cats may develop LUTS. These cats are often diagnosed with FIC after excluding other potential causes of LUTS. Individual susceptibility to FIC appears to exist, and understanding the concept that clinical expression of episodes of FIC occur when the combination of individual susceptibility and deficient environmental factors exceeds a certain threshold is important for long-term management ***(Figure 3)***.

While the individual susceptibility is "fixed" for a specific cat, efforts must be made to eliminate or reduce potential negative environmental or social factors ***(Figure 4)*** and MEMO helps to achieve this goal. Some cats might only need one apparently minor alteration to ensure no further episodes of LUTS, while hard-to-treat cats may require many changes to limit FIC episodes to an acceptable level. As noted above, for some cats with FIC a detailed individual history to identify potential risk factors may be necessary to be successful in the long-term management of this disease. While published risk factors ***(Table 1)*** can give some guidance for history taking, many other triggers can affect specific cats and it might be essential to identify and manage these aspects in some cases. Consulting a behaviorist is advisable in hard-to-treat cases.

Other treatment considerations

During acute non-obstructive episodes, analgesics such as buprenorphine (10-30 µg/kg given orally (transmucosally) q8H) and/or non-steroidal anti-inflammatory drugs (NSAIDs) (*e.g.*, meloxicam 0.1 mg/kg PO q24H on day 1, followed by 0.05 mg/kg q24H for up to 1 week) should be considered to relieve discomfort, assuming there are no medical contraindications. Note that any long-term treatment with NSAIDs is discouraged because there is no evidence-based beneficial effect. Emergency management and medical treatment for cats with urethral obstructions is reviewed by another paper in this issue.

The use of additional medical treatments for long-term control should only be considered when MEMO and increased water intake are insufficient to prevent periodic episodes of FIC. The use of feline facial pheromone therapy, amitriptyline, and glycosaminoglycans are all options to consider in chronic recurrent cases, but none should be started immediately after diagnosis of FIC because their effectiveness has not yet been proven compared with MEMO and water management.

CASE STUDY N°1

A typical presentation of FIC

Amadeo is a 4-year-old male castrated domestic shorthair presented because of 3 previous episodes of LUTS (mainly pollakiuria and hematuria) within the last year, each lasting between 3 and 10 days, and a new episode at presentation. The owner felt that Amadeo was a generally anxious and stressed cat, hiding from anything and anyone unknown. The cat was fed a struvite preventative dry diet to encourage diuresis (based on a previous urinalysis that showed moderate struvite crystalluria, severe hematuria, and a mild pyuria with a negative bacterial culture). Abdominal radiography, performed during the last episode, showed no anomalies.

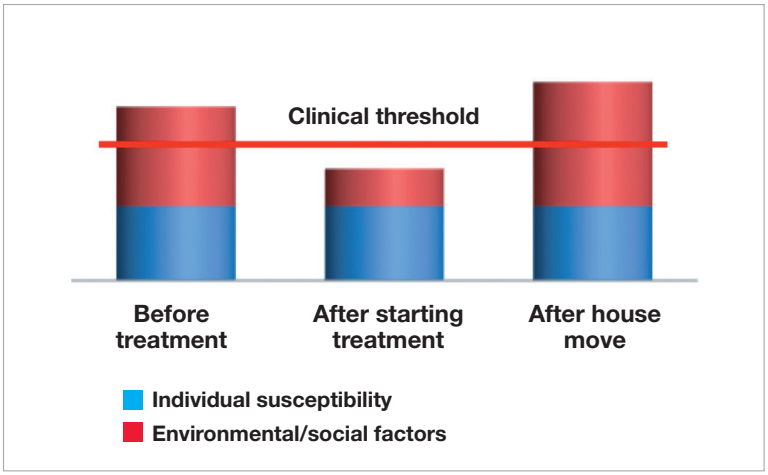


Figure 4. Clinical disease expression of feline idiopathic cystitis in case 1. After increasing water intake by providing different water sources and changing from dry to canned food, and after allowing restricted outdoor access with subsequent increased activity and minor weight loss, the cat showed no further clinical signs of FIC as he remained below the clinical threshold. During follow-up however, the owners moved house, and at this point there was a minor relapse of clinical FIC because the clinical threshold had been exceeded. Lifelong management is necessary for a subgroup of cats with FIC.

Other than a BCS of 6/9 and signs of stress (tachypnea, bilateral mydriasis), no physical anomalies were found on examination. A small, apparently non-painful urinary bladder was palpated.

Considering the signalment, history, and previously performed diagnostics, FIC was the most likely diagnosis. Because of the recurring episodes, the owner preferred additional examinations to exclude much less likely causes (*e.g.,* radiolucent uroliths). Abdominal ultrasound demonstrated a diffuse, mildly thickened urinary bladder wall and a lot of sediment in the bladder lumen. No evidence of any other cause of LUTS was found, so the diagnosis of FIC was confirmed.

Detailed history taking identified several potential risk factors: namely no outdoor access, overweight, dry diet only, and presence of another cat in the same household, while only one bowl of food and water, and only one litter box was employed. Amadeo was gradually switched from the dry to the canned form of the same struvite preventative diet. A water fountain was introduced, and several litter boxes, food and water bowls were placed at different locations in the house. Restricted outdoor access was also provided. Until the episode of LUTS was over, buprenorphine was also given orally for 4 days. Interpretation of disease expression and follow-up are shown in ***Figure 4***.

CASE STUDY N°2

An example of possible pitfalls in the diagnosis of cats with LUTS

Figo is a 7-year-old male castrated Persian who presented with a 2-week history of dysuria, stranguria and hematuria. During this period the cat was always able to evacuate regular small amounts of urine and he had never showed any signs of LUTS previously. Other clinical anomalies in the history were absent. The referring veterinarian had performed an abdominal ultrasound which found no relevant anomalies, and had treated with NSAIDs, buprenorphine, and antibiotics (cephalexin) without clinical improvement. A urethral catheterization was also performed without any resistance. The cat was bright, alert, and responsive at presentation. The only anomaly on physical examination was a small, painful urinary bladder.

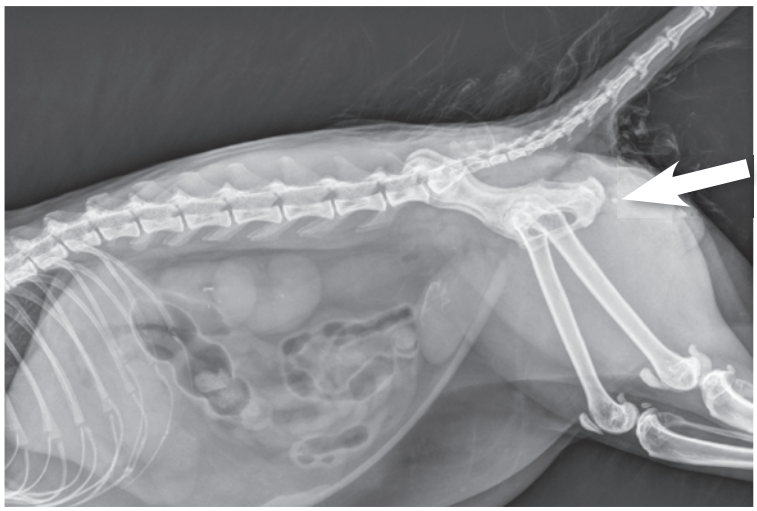


Figure 5. Lateral abdominal radiograph of Figo. A urethral stone caudal to the ischium was detected (arrowed). Also note the presence of renal and bladder wall calcifications.

The major differentials for LUTS in this case were FIC, urolithiasis (urethrolithiasis was more likely, considering the normal urinary bladder ultrasound from the referring vet), and UTI (considering the previous catheterization). Other differentials were considered unlikely in this case.

The diagnostic plan included urinalysis + culture by cystocentesis, and plain abdominal radiography. Urine sediment analysis revealed no crystals or bacteria, 24 wbc/hpf, and >100 rbc/hpf. Urine culture was negative. The lateral abdominal radiograph showed the presence of a well-defined mineralized oval opacity at the level of the urethra caudal to the ischium ***(Figure 5)*** and a urethral calculus was diagnosed.

Before surgical intervention, general blood analysis was performed and did not identify any anomalies. Retrograde urohydropropulsion, followed by cystotomy, was performed. A 3 mm urolith was removed from the urinary bladder. Recovery was uneventful, and quantitative stone analysis diagnosed calcium oxalate urolithiasis. A preventative diet was initiated, and the cat did not show any relapse during follow-up.

If the work-up had been limited to urinalysis, urine culture, and abdominal US, this cat would have been misdiagnosed with FIC. This case highlights the importance of plain abdominal radiographs, which should include the entire urethra. Even where there is no obvious evidence of urethral obstruction in the history/physical examination, radiography should be the first imaging modality to be performed. This case also shows that "not feeling" a urethral stone during catheterization does not exclude the presence of a urethrolith.

Outcome

A “cure” for FIC does not exist. However, current individually tailored treatment approaches (water and environmental management) can reduce or prevent new episodes of FIC in most cats. Many cats with a relatively low individual susceptibility may only present with one episode of LUTS and never have recurring signs again, even without long-term management. The most difficult cats to treat are often those with recurrent urethral obstructions over a short period, when there is sometimes insufficient time to implement appropriate management changes; in these cases surgical intervention can be necessary. The risk of death from urethral obstructions and the possibility of elective euthanasia because of recurring LUTS makes appropriate long-term management essential in cats with a higher susceptibility.

References

1. Kruger JM, Osborne CA, Goyal SM, *et al.* Clinical evaluation of cats with lower urinary tract disease. *J Am Vet Med Assoc* 1991;199:211-216.
2. Osborne CA, Kruger JM, Lulich JP. Feline lower urinary tract disorders. Definition of terms and concepts. *Vet Clin North Am Small Anim Pract* 1996; 26:169-179.
3. Buffington CAT, Chew DJ, Kendall MS, *et al.* Clinical evaluation of cats with non-obstructive urinary tract diseases. *J Am Vet Med Assoc* 1997;210: 46-50.
4. Lekcharoensuk C, Osborne CA, Lulich JP. Epidemiologic study of risk factors for lower urinary tract diseases in cats. *J Am Vet Med Assoc* 2001;218: 1429-1435.
5. Gerber B, Boretti FS, Kley S, *et al.* Evaluation of clinical signs and causes of lower urinary tract disease in European cats. *J Small Anim Pract* 2005;46: 571-577.
6. Sævik BK, Trangerud C, Ottesen N, *et al.* Causes of lower urinary tract disease in Norwegian cats. *J Feline Med Surg* 2011;13:410-417.
7. Rossi M, Messina N, Ariti G, *et al.* Symptomatic *Capillaria plica* infection in a young European cat. *J Feline Med Surg* 2011;13:793-795.
8. Westropp JL, Buffington CAT. Feline idiopathic cystitis: current understanding of pathophysiology and management. *Vet Clin North Am Small Anim Pract* 2004;34:1043-1055.
9. 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.
10. Buffington CAT, 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.
11. Cameron ME, Casey RA, Bradshaw JW, *et al.* A study of environmental and behavioural factors that may be associated with feline idiopathic cystitis. *J Small Anim Pract* 2004;45:144-147.
12. Defauw PA, Van de Maele I, Duchateau L, *et al.* Risk factors and clinical presentation of cats with feline idiopathic cystitis. *J Feline Med Surg* 2011;13:967-975.
13. Forrester DS, Roudebush P. Evidence-based management of feline lower urinary tract disease. *Vet Clin North Am Small Anim Pract* 2007;37:533-558.

Epidemiology - characteristics of cats diagnosed with cystitis

Sandi Lefebvre, DVM, PhD
Banfield Pet Hospital, Portland, Oregon, USA

Dr. Lefebvre joined Banfield in 2011 as Associate Medical Advisor – Research for the Banfield Applied Research and Knowledge (BARK) team. A 2003 graduate of Ontario Veterinary College, she obtained her PhD in epidemiology through research and development of guidelines for pet visitation in human hospitals. Her most recent professional role was as scientific editor for *JAVMA* and *AJVR*.

Introduction

Feline lower urinary tract disease (FLUTD) is a syndrome with multiple causes including urolithiasis, urinary tract infection, neoplasia, and other urologic anomalies (1), although in most affected cats the cause remains unidentified and a diagnosis of feline idiopathic cystitis (FIC) is made (2). Pyuria is typically minimal in cats with idiopathic cystitis (3) and failure to detect white blood cells on urine sediment examination can generally be used to discern FIC from bacterial cystitis. The present study was conducted to characterize the clinical features of a large population of feline patients diagnosed with cystitis at primary care veterinary practices in the United States.

Method of analysis

Feline patients at 815 Banfield Pet Hospitals in 43 states were considered eligible for the study when they had an incident (first-ever) diagnosis of "cystitis", the main code by which idiopathic cystitis would be recorded in the electronic medical records system, at some point in 2012. Included cats were also required to have had a urinalysis performed at the time of diagnosis, with urine collected via cystocentesis. Data extracted from the medical records included age, clinical signs and body condition at the time of diagnosis, sex, reproductive status, breed, and results of physical examination and urinalysis.

Summary statistics were calculated. The Chi-square test was used to compare the proportions of cats that had cystitis with those in the general population with respect to various factors. Values of $P < 0.05$ were considered significant.

Results

From a total of 456,717 cats seen at Banfield in 2012, 16,082 (3.5%) had an incident diagnosis of cystitis. Of these cats, 8,220 (51.1%) had concurrent pyuria (white blood cells detected via urine sediment examination). The median age of cats with pyuria was 6.1 years (range 0.3-23.3 years), and for cats without pyuria 5.7 years (range, 0.3 - 24.0 years).

Clinical features of cats with cystitis are summarized in ***Table 1*** by presence or absence of pyuria. Among cats with pyuria, neutered males (n = 3,999 [48.7%]) and spayed females (3,839 [46.7%]) were over-represented with respect to their distribution in the general patient population (36.5% and 36.6%, respectively; $P < 0.001$), and the same was true for cats without pyuria (3,563 neutered males [45.3%] and 3,809 spayed females [48.5%]).

All domestic breeds (short, medium and longhair) as well as Siamese, Maine Coon, and Persians were over-represented ($P < 0.001$) with respect to their distribution in the general patient population, whether pyuria was present or not. There were also significantly ($P < 0.001$) greater proportions of cats fed dry diets and overweight cats in both cystitis groups than in the general patient population.

For comparison, of all cats seen at Banfield in 2012, 23.2% were overweight or obese. Breed distributions in the general patient population were as follows: DSH, 13.9%; DMH, 2.5%; DLH, 1.9%; Siamese, 0.7%; Maine Coon, 0.3%; and Persian, 0.3%. Diet distribution in the general population of cats (for which data were available)

Table 1. Clinical features of cats diagnosed with cystitis with (n = 8,220) or without (7,862) concurrent pyuria in 2012.

Feature	No. (%) with pyuria	No. (%) without pyuria
Overweight or obese	2,467 (30.0)	2,172 (27.6)
Underweight	548 (6.7)	379 (4.8)
Inappropriate elimination	183 (2.2)	126 (1.6)
Stranguria or dysuria	16 (0.2)	32 (0.4)
Anorexia	9 (0.1)	7 (0.09)
Depressed mentation	6 (0.07)	3 (0.04)
Bradycardia	0 (0)	2 (0.03)
Hypothermia	1 (0.01)	6 (0.08)
Hyperkalemia	112 (1.4)	152 (1.9)
Hematuria	7,160 (87.1)	2,073 (26.4)
Bacteriuria	6,245 (76.0)	1,877 (23.9)
Urolithiasis or nephrolithiasis	76 (0.9)	48 (0.6)
Breed		
DSH	5,287 (64.3)	5,139 (65.4)
DMH	970 (11.8)	896 (11.4)
DLH	882 (10.7)	788 (10.0)
Siamese	311 (3.8)	270 (3.4)
Maine Coon	171 (2.1)	158 (2.0)
Persian	131 (1.6)	116 (1.5)
Diet*		
Canned only	48 (3.5)	49 (3.7)
Dry only	1,055 (77.3)	993 (75.7)
Mixed canned and dry	262 (19.2)	269 (20.5)

*Data on diet were available for 1,365 cats with pyuria and 1,311 cats without pyuria.

was as follows: canned only, 4.5%; dry only, 66.0%; and mixed, 29.5%.

Discussion

The risk of cystitis with or without pyuria was higher in cats that were sterilized, overweight, fed dry diets, or of specific breeds. These findings are consistent with those of other studies of FLUTD (2,4). Other findings highlight the challenge in discerning the cause of FLUTD, as clinical features such as stranguria/dysuria or hematuria were shared by all cats, regardless of whether or not they had pyuria. For this reason, a complete diagnostic work-up, including at minimum a detailed history, complete physical examination, urinalysis, and hematologic evaluation is strongly recommended for any cat in which FLUTD is suspected.

References

1. Grauer GF. Feline lower urinary tract disease. In: Nelson RWC, Couto C G, eds. *Small Animal Internal Medicine*. 4th ed. St. Louis, MO: Mosby Elsevier; 2009;677-683.
2. Lekcharoensuk C, Osborne CA, Lulich JP. Epidemiologic study of risk factors for lower urinary tract diseases in cats. *J Am Vet Med Assoc* 2001;218(9):1429-1435.
3. Hostutler RA, Chew DJ, DiBartola SP. Recent concepts in feline lower urinary tract disease. *Vet Clin Small Anim* 2005;35(1):147-170.
4. Jones BR, Sanson RL, Morris RS. Elucidating the risk factors of feline lower urinary tract disease. *N Z Vet J* 1997;45(3):100-108.

Urinary relative supersaturation and urolithiasis risk

Yann Quéau, DVM, Dipl. ACVN
Royal Canin Research Center, Aimargues, France

Dr. Quéau graduated from the National Veterinary School of Toulouse (France) in 2007 after completing a veterinary thesis on the effect of aging on the glomerular filtration rate in dogs. Following graduation he completed an internship in Renal Medicine and Hemodialysis, and a residency in Small Animal Clinical Nutrition, at the University of California, Davis. He became a Diplomate of the American College of Veterinary Nutrition in 2011, and currently works at the Royal Canin Research Center in Aimargues, France.

Vincent Biourge, DVM, PhD, Dipl. ACVN, Dipl. ECVCN
Royal Canin Research Center, Aimargues, France

Dr. Biourge graduated from the Faculty of Veterinary Medicine of the University of Liège (Belgium) in 1985. He stayed as an assistant in the nutrition department for two years before moving to the Veterinary Hospital of the University of Pennsylvania (USA) and later to the Teaching Hospital of the University of California, Davis as a PhD/resident in clinical nutrition. In 1993 he received his PhD in Nutrition and became a Diplomate of the American College of Veterinary Nutrition. In 1994 he joined Royal Canin's Research Center in Aimargues as nutritionist and head of scientific communication. Between 1999 - 2007 he was in charge of managing the nutritional research programs; since 2008 he has held the post of Health & Nutrition Scientific Director.

Introduction

Urinary stones represent 18% and 15% of all lower urinary tract diseases in dogs and cats respectively (1). In various veterinary stone analysis laboratories, dogs account for 72-81% of total stone submissions, much more than cats (2-4). Struvite and calcium oxalate (CaOx) uroliths represent 80-90% of all stones in both species, but data from North America and Europe show that relative proportions of each type have varied over the years. Struvite predominated in the 1980s, but was progressively outnumbered by calcium oxalate in the mid-1990s. An inverse shift has now been reported in the last few years (2,5-7).

KEY POINTS

- **Relative supersaturation (RSS) remains to date the best tool to assess the risk of crystal formation in urine. It is used to optimize diet formulations, but is unfortunately too cumbersome to be measured in a clinical setting.**
- **Data obtained in healthy dogs and cats show that urinary pH is an important determinant of struvite RSS, but not calcium oxalate RSS.**
- **Urinary pH should be interpreted with caution by practitioners when assessing patients at risk for urolithiasis, due to within-day variability and the poor correlation with calcium oxalate RSS.**
- **Increasing dietary sodium or moisture is effective in decreasing RSS of both struvite and calcium oxalate. Urine specific gravity can be used by practitioners to monitor patients at risk of urolithiasis.**

Veterinarians in practice have limited access to urine samples and tools when it comes to assessing the risk of an animal forming uroliths. Urine specific gravity (USG) and pH, as well as microscopic examination of the sediment to visualize crystals, are frequently performed on "spot" urine samples, and while they can be informative, such tests are unfortunately imperfect when considering the risk of various types of urolithiases. For instance, stones can be present when visualized crystals are absent (and vice-versa), and urine pH varies greatly over the course of the day (8). This paper reviews the relationship between urinary relative supersaturation (RSS) and the risk of urolithiasis in dogs and cats, and identifies recent advances in this area.

Why use relative supersaturation?

Supersaturation of the urine is the physico-chemical prerequisite for stones to develop. In this state, crystal-

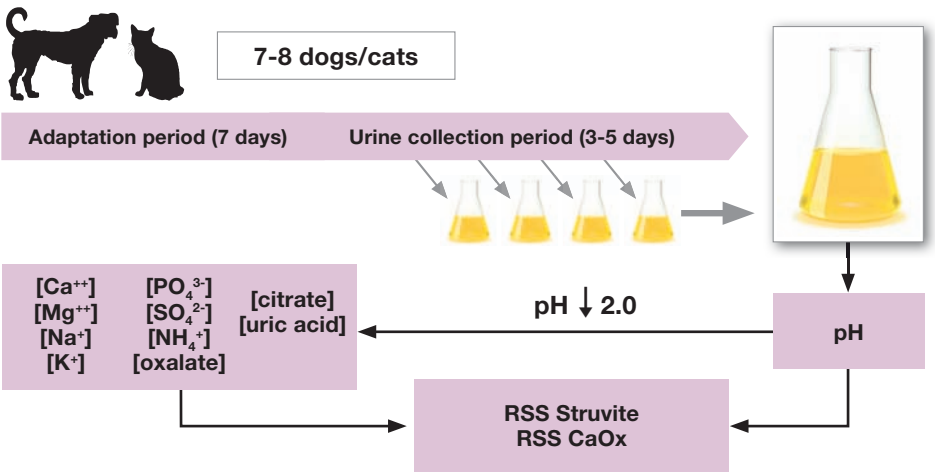


Figure 1. Schematic representation of the protocol currently used at the Royal Canin Research Center to obtain representative urine samples for RSS.

lization can occur because the concentration of the crystallizing ions is higher than their solubility product (*i.e.*, the concentration at which the components of a crystal will precipitate in a solvent (like water), at a defined temperature, and - depending on the nature of the crystals - a defined pH). The degree of supersaturation affects crystal nucleation, growth and aggregation, the three steps that precede the formation of macroscopic stones. Therefore the degree of urine supersaturation for a given crystal (*e.g.,* calcium oxalate) is a good indicator of the risk that formation of this salt will occur in the urine, although it does not take into account some other influences such as the presence of organic promoters or inhibitors of crystallization. Estimation of urinary RSS was the most widely used and recognized method in human medicine until less expensive prediction models became available, and RSS has now been used for more than a decade in dogs and cats after validation in these species (9).

Methodology: how to evaluate and interpret RSS

Animal phase

To be relevant, RSS must be estimated on a representative urine sample. In humans, one or two 24-hour urine collections are required for comprehensive metabolic evaluation of patients and for RSS calculation (10). In dogs and cats fed canned diets, 48-hour urine collection periods have been described when performing pH monitoring and RSS estimation (11,12), as urine can be more concentrated than in humans. When dry diets are fed, even longer collection periods (*e.g.*, 72 hours) may be necessary if the diets are not specifically formulated to increase diuresis.

The protocol currently used at the Royal Canin Research Center (as approved by the Ethics Committee) to obtain representative urine samples is shown schematically in ***Figure 1***. Briefly, urine is collected from individual animals by a non-invasive method for at least 72 hours (after the animals have had 7 days of adaptation to the new diet). The individual urine samples are then pooled and stored at 4°C; pH is measured and then adjusted to 2.0 with hydrochloric acid in order to dissolve all salts before ion concentrations are determined.

Analytical phase and RSS calculation

The concentrations of calcium, phosphate, magnesium, sodium, potassium, ammonium, oxalate, citrate, sulfate and uric acid in the urine pool are measured by ionic chromatography; all of these are required to calculate the RSS of a given urine sample. Various computer software packages have been developed and validated for both dogs and cats, allowing RSS to be calculated from the urinary concentrations and urine pH (9). Urine pH is required for the calculation as it influences the form in which certain ions will be present; the overall effect of pH on RSS will be discussed later.

Briefly, the computer program determines the concentrations of the solutes that remain free to interact (the activity products) to form various crystals - including calcium oxalate and struvite - taking into account all possible interactions between the ions and the complexes that could be formed. These activity products are then compared to the solubility products (see above) of the given salt to predict whether the urine is undersaturated or supersaturated for this salt. The ratio is known as the RSS ***(Figure 2)***.

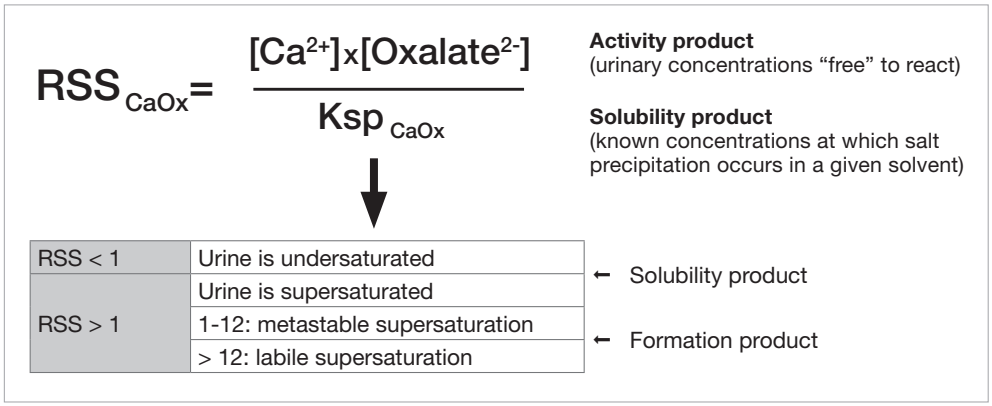


Figure 2. Calculation and interpretation of RSS values. The example is given for calcium oxalate, but the principle is identical for other salts such as struvite (magnesium ammonium phosphate) or calcium phosphate. Only solubility and formation products can vary according to the salt.

Interpretation

Based on the average RSS value of the animals in a test panel, it can be concluded whether a specific diet has the potential to induce undersaturated or supersaturated urine. If the urine is undersaturated for a given salt (*e.g.,* struvite), crystals will dissolve. On the other hand, supersaturated urine does not always lead to stone formation. Indeed, the supersaturation state is not uniform: it can be metastable or labile (unstable). In the metastable zone, spontaneous crystallization does not occur as it requires a nucleus to grow, while in the labile (unstable) zone, crystallization does occur. The RSS limit value between those two states is defined as the formation product of the given salt.

RSS and diet testing

After 15 years of experience with RSS and diet testing, the definitive conclusion is that RSS is more accurate than urinary pH when assessing the risk factors for urolithiasis.

Struvite

Struvite stones have long been known to be affected by urinary pH. Indeed, in an acid urine environment, phosphate ions (PO_4^{3-}) within the struvite stones are protonated (HPO_4^{2-}, $H_2PO_4^-$, H_3PO_4), making them unavailable to form complexes with ammonium and magnesium. Various studies and epidemiological observations have led to the classical recommendation that diets which induce a urine pH of < 6.5 should be fed. RSS studies at the Royal Canin Research Center have allowed refinement of this relationship between pH and the risk of struvite formation. Derived from multiple feeding trials in adult cats over several years, the relationship between struvite RSS and urinary pH is shown in ***Figure 3***.

As can be seen, very acid urine (pH < 6.2) always promotes RSS values in the undersaturated zone, which is favorable for struvite prevention and dissolution. For the classically recommended pH range (6.2-6.5), RSS values are either in the undersaturated or metastable supersaturated zone for dry diets, allowing prevention of spontaneous struvite crystallization under controlled conditions (*i.e.,* absence of urinary tract infection or preformed crystal nuclei). Results for pH > 6.5 are much more variable. Some cats with very alkaline urine still maintain undersaturated urine, which can be explained by the other determinants of RSS calculation, the ion concentrations. Indeed, with conditions that promote urine dilution, as in moist diets (wet food), urine pH becomes less critical.

The fact that RSS is a better predictor of struvite dissolution has been demonstrated in *ex vivo* dissolution studies. Such studies showed that with identical urine pH and struvite stone shapes and weights, a lower RSS promoted a more rapid dissolution, whereas dissolution times were identical in urines with similar RSS but different pH (13).

It should be emphasized that unlike cats, dogs almost always develop struvite stones secondary to urinary tract infections with urea-splitting bacteria (*Klebsiella, Proteus, Pseudomonas, Staphylococcus* and *Mycoplasma*) (14). In this situation the diet alone, even if shown to promote a low RSS in healthy dogs, will not be sufficient to dissolve and prevent recurrence of struvite stones if the infection is not appropriately and concurrently controlled ***(Figure 4)***. The rare occurrence of canine sterile struvite stones (only described so far in one family of cocker spaniels (15)) might be explained by a lesser ability of dogs compared to cats to concentrate urine.

Calcium oxalate

The role of pH in calcium oxalate urolithiasis is more controversial. It has been suggested that acidifying diets

increase the risk of CaOx stone formation, based on epidemiological data (16) and the reciprocal shifts between struvite and CaOx stone prevalence over the years. One of the predominant hypotheses is that promotion of acid urine also promotes calciuria and reduces citraturia, both factors potentially favoring CaOx crystallization.

However, CaOx RSS measurements obtained over the years do not support a strong association with urinary pH ***(Figure 5)***. A recent prospective study showed that in cats, gradual acidification of a basal diet which altered the pH from 6.4 to 5.9 increased calcium excretion in the urine, but the RSS remained unchanged (17). It is possible that a much higher pH may be effective, as suggested by one study (18) where the effect on CaOx supersaturation was seen over a broader range of pH values (up to 7.9), but not for moderately acid urine as commonly induced by most maintenance and urinary feline diets. Based on those data, it appears that diets can successfully be formulated to induce a urine pH allowing undersaturation for struvite, with no detrimental effect on CaOx RSS.

RSS and dilution

Increased levels of dietary salt have been used to stimulate water intake and promote urine dilution. The lower urinary ion concentration resulting from this strategy decreases RSS, as evidenced by several studies in dogs and cats (19-21). In dogs, raising the sodium level of a dry expanded diet from 0.5 to 3.0 g/1000 kcal significantly increased water intake and decreased CaOx RSS (19). The same effect was observed in dogs when the sodium was increased from 0.6 to 3.0 g/1000 kcal in a canned diet (20). It is important to distinguish dry from wet diets, as dietary moisture also affects urine concentration and therefore CaOx RSS. In a study with miniature schnauzers and Labrador retrievers comparing two diets that differed only in their moisture content, the 73% moisture diet resulted in lower USG, oxalate concentration and RSS than the 7% moisture diet in the schnauzers (19). Those changes were not significant in Labradors, which had higher urinary volumes and lower urine concentration than the schnauzers regardless of diet.

Similarly in cats fed four diets that differed only in moisture content (6%, 25%, 53% and 73%), the 73% moisture diet resulted in a higher water intake, lower USG and lower CaOx RSS than the other diets (22). This latter study also underlines that the effect of moisture on urine dilution is only obtained with a high level of moisture. Dietary strategies to promote urine dilution in order to

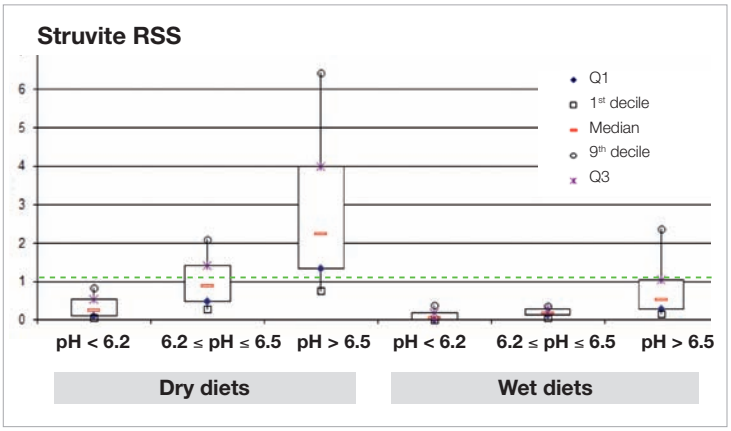
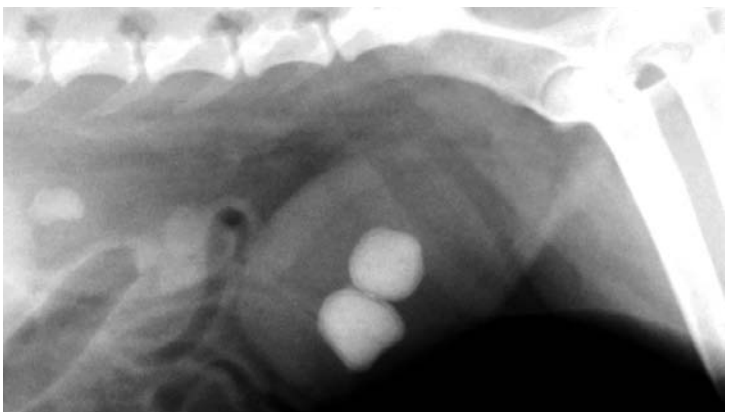


Figure 3. The relationship between struvite RSS and urinary pH in 142 cats fed dry (n = 481) and wet (n = 27) diets. The green dashed line represents the solubility product for struvite (the limit between the undersaturated and the supersaturated zones).



© Dr. William Widmer

Figure 4. Struvite uroliths are radiopaque and thus can be seen on technically correct survey radiographs. Note that even if a diet promoting a low RSS is fed, this will not be sufficient to dissolve and prevent recurrence of the stones if the concurrent bacterial infection is not appropriately controlled.

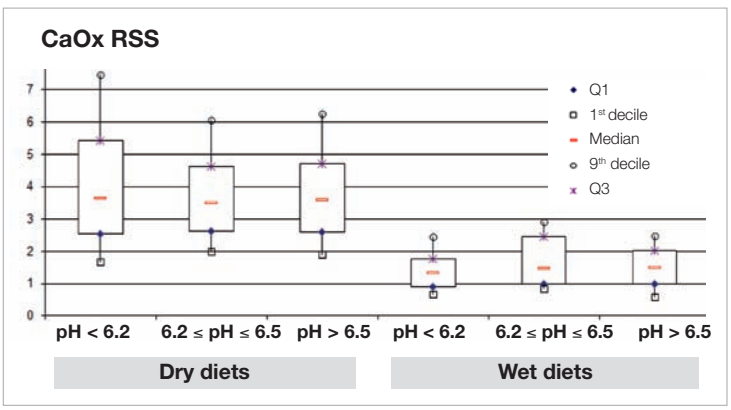


Figure 5. The relationship between CaOx RSS and urinary pH is less well-defined (Data obtained from the same cat population as ***Figure 3***).

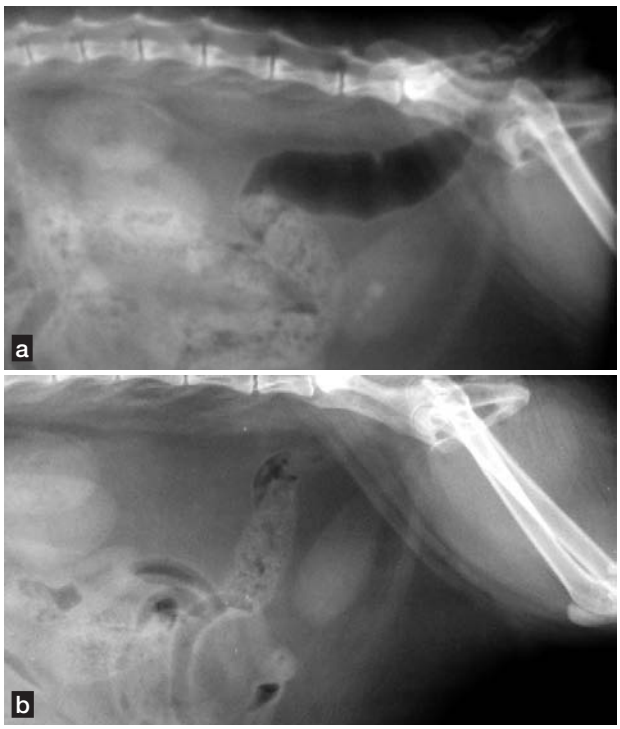


Figure 6. Radiographs of a cat with suspected struvite uroliths in the bladder before **(a)** and after **(b)** 15 days on a diet (wet or dry) formulated to induce a RSS < 1. At day 15, the uroliths are no longer visible (25).

decrease CaOx RSS have been supported by studies in both dog (23) and cat (24) stone formers, although more data is required in those populations.

How can the practitioner use these results?

From the data, it can be concluded that urine pH and USG provide only limited information to the practitioner in estimating the risk of stone formation or recurrence in a patient. Those parameters can however provide some insight in specific situations:

- A fasted urine pH < 6.2 in a cat indicates a low risk of struvite stone formation, since most RSS values will be under the formation product below this pH.
- A fasted urine pH > 6.5 is not always indicative of a high risk of struvite crystalluria, especially in animals fed canned diets that promote urine dilution.
- A urine pH obtained in the hours following a meal can be elevated and unrepresentative of the average urine pH, due to the postprandial alkaline tide. A pH measurement obtained after a night of fasting is more relevant, but ideally urine should be collected for at least 48 to 72 hours.
- Urinary pH is not a good predictor of CaOx RSS.
- USG, a marker of urine dilution, remains a good, although imperfect, tool to assess the relative risk of stone formation, especially during follow-up of stone formers to prevent recurrence. The thresholds classically recommended (< 1.020 in dogs and < 1.025 in cats) can be difficult to achieve in some instances (*e.g.,* in cats fed a dry diet).
- It is possible to formulate diets that will both promote the dissolution of struvite stones and low urinary saturation of struvite and CaOx.

RSS: how it translates to *in vivo* observations

While RSS is obtained from analyses run on urine samples obtained *in vivo*, and describes physicochemical reactions occurring in the urine, it can be argued that this risk index does not take into account other factors known to influence the different crystallization steps, such as organic promoters or inhibitors. Therefore the question of its relevance and accuracy to predict stone formation *in vivo* can be raised. This is partially answered by studies in humans and animals; both stone-forming humans and dogs (especially those with recurrent CaOx or calcium phosphate uroliths) have higher corresponding RSS values than healthy individuals, despite overlap between the two groups (9,23). A recent study has demonstrated the validity of using a diet known to induce a struvite RSS < 1 to predict and achieve struvite stone dissolution in cats (25) ***(Figure 6)***.

Another potential limit of RSS measured in research centers is the health status of the animals studied. Metabolic differences between animal populations may explain the appearance of the disease and could affect the RSS value. However, it is difficult to obtain and process 48-hour urine samples in privately-owned animals for RSS. Studies in both dogs (23) and cats (24) not only showed that stone formers have higher CaOx RSS on their usual diet compared to healthy animals, but that when fed diets promoting urine dilution the CaOx RSS decreased, and also that (in dogs) feeding such diets for a year was not associated with clinical recurrence of uroliths.

Conclusion and perspectives

Today, RSS remains the best tool to predict the potential for a diet to induce urinary stone formation or dissolution. Several years of research in this field in cats and dogs have allowed a better comprehension of the limitations in using urinary pH as the sole risk factor for urolithiasis (especially CaOx), and assessment of the effect of urinary dilution (via dietary sodium or moisture)

on the risk of stone formation, amongst other findings. However, more research is still needed, especially when it comes to understanding the effect of specific nutrient modifications on urine composition and RSS, and to investigate the metabolic differences between normal animals and stone formers.

References

1. Houston DM, Moore AE, Elliott DA, *et al*. Stone diseases in animals. In: Rao NP, Preminger GM, Kavanagh JP, eds. *Urinary Tract Stone Disease*. Warrington, PA: Springer; 2011:131-150.
2. Osborne CA, Lulich JP, Kruger JM, *et al*. Analysis of 451,891 canine uroliths, feline uroliths, and feline urethral plugs from 1981 to 2007: perspectives from the Minnesota Urolith Center. *Vet Clin North Am Small Anim Pract* 2009;39:183-197.
3. Houston DM, Moore AE. Canine and feline urolithiasis: examination of over 50 000 urolith submissions to the Canadian veterinary urolith centre from 1998 to 2008. *Can Vet J* 2009;50:1263-1268.
4. Rogers KD, Jones B, Roberts L, *et al*. Composition of uroliths in small domestic animals in the United Kingdom. *Vet J* 2011;188:228-230.
5. Picavet P, Detilleux J, Verschuren S, *et al*. Analysis of 4,495 canine and feline uroliths in the Benelux. A retrospective study: 1994-2004. *J Anim Physiol Anim Nutr (Berl)* 2007;91:247-251.
6. 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;231:570-576.
7. Low WW, Uhl JM, Kass PH, *et al*. Evaluation of trends in urolith composition and characteristics of dogs with urolithiasis: 25,499 cases (1985-2006). *J Am Vet Med Assoc* 2010;236:193-200.
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. 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-1641S.
10. Semins MJ, Matlaga BR. Blood and urinary tests in stone formers. In: Rao NP, Preminger GM, Kavanagh JP, eds. *Urinary Tract Stone Disease*. Warrington, PA: Springer; 2011:369-374.
11. Stevenson AE, Smith BH, Markwell PJ. A system to monitor urinary tract health in dogs. *J Nutr* 1998;128:2761S-2762S.
12. Markwell PJ, Smith BHE, McCarthy K. A non-invasive method for assessing the effect of diet on urinary calcium oxalate and struvite supersaturation in the cat. *Animal Tech* 1999;50:61-67.
13. van Hoek I, Malandain E, Tournier C. RSS is a better predictor for struvite dissolution than urine pH. *Vet Focus* 2009;19(2):47-48.
14. Osborne CA, Lulich JP, Polzin DJ, *et al*. Medical dissolution and prevention of canine struvite urolithiasis. Twenty years of experience. *Vet Clin North Am Small Anim Pract* 1999;29:73-111.
15. Bartges JW, Osborne CA, Polzin DJ. Recurrent sterile struvite urocystolithiasis in three related cocker spaniels. *J Am Anim Hosp Assoc* 1992;28:459-469.
16. 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.
17. Quéau Y, Hoek I, Feugier A, *et al*. Urinary pH affects urinary calcium excretion but not calcium oxalate relative supersaturation in healthy cats. *J Vet Intern Med* 2013;27:738-739.
18. Jeremias JT, Loureiro BA, Maria APJ, *et al*. Effect of food base excess on body mineral balance and urinary relative supersaturation for calcium oxalate in adult cats. In *Proceedings* 16th ESVCN Congress 2012:65.
19. Stevenson AE, Hynds WK, Markwell PJ. Effect of dietary moisture and sodium content on urine composition and calcium oxalate relative supersaturation in healthy miniature schnauzers and Labrador retrievers. *Res Vet Sci* 2003;74:145-151.
20. Lulich JP, Osborne CA, Sanderson SL. Effects of dietary supplementation with sodium chloride on urinary relative supersaturation with calcium oxalate in healthy dogs. *Am J Vet Res* 2005;66:319-324.
21. Hawthorne AJ, Markwell PJ. Dietary sodium promotes increased water intake and urine volume in cats. *J Nutr* 2004;134:2128S-2129S.
22. 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:S128-130.
23. 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;5:218-231.
24. 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.
25. 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:S90-92.

HOW I TREAT...

The cat with a blocked bladder

Edward Cooper, VMD, MS, DipI. ACVECC
Department of Veterinary Clinical Sciences, The Ohio State University, Columbus, USA

Dr. Cooper graduated from the University of Pennsylvania School of Veterinary Medicine in 2002 before following a rotating internship at Michigan State University. He completed an emergency medicine internship at the University of Pennsylvania and an emergency/critical care residency at the Ohio State University. He is a Diplomate of the American College of Veterinary Emergency and Critical Care and an Associate Professor at Ohio State. His research interests include urethral obstruction in cats including shock, fluid resuscitation, and hemodynamic monitoring.

Pathogenesis of obstruction

Urethral obstruction (UO) is a potentially life-threatening manifestation of feline lower urinary tract disease. The male cat has a long and narrow urethra (compared to the female), and is much more likely to develop an obstruction. It has long been held that the presence of a physical obstruction, such as a calculus or urethral plug (or much less commonly stricture or neoplasia), is responsible for occluding the lumen of the urethra in these cases, but there is evidence to suggest that mechanical obstruction secondary to urethral spasm and edema may play an equally important role (1,2). These conditions are thought to be brought about by underlying feline idiopathic cystitis (FIC). The pathogenesis of FIC is still unclear but it appears to be a sterile inflammatory process, as attempts to consistently isolate a bacterial or viral cause have been unsuccessful.

Instead, extensive investigation into neurohumoral alterations in cats with FIC has demonstrated that the disease may be related to an imbalance between the sympathetic nervous system and the hypothalamic-pituitary-adrenal axis brought about by stressful situations (3). This imbalance is thought to result in impaired blood flow and release of inflammatory mediators which cause edema, smooth muscle spasm and pain within the lower urinary tract. Pain, in turn, can contribute to the escalation of urethral smooth muscle dysfunction and urethral inflammation, thereby creating a vicious cycle. These conditions, either independently or in conjunction with a physical obstruction such as a plug or a stone, ultimately lead to urethral obstruction in cats.

KEY POINTS

- **Feline urethral obstruction may occur secondary to physical obstruction (stones, mucous plug) as well as functional obstruction (inflammation, urethral spasm, edema).**
- **Heavy sedation, lubricated flush, and appropriate technique are essential to ensure the risk of urethral trauma is minimized.**
- **Severe hyperkalemia is considered to be the most life-threatening aspect of obstruction.**
- **Awareness and monitoring for post-obstructive diuresis is important to maintain appropriate fluid balance.**
- **Analgesia and urethral relaxants are important components of therapy both during hospitalization and after discharge.**

Pathophysiology of obstruction

Complete obstruction of the urethra leads to the accumulation of urine and pressure within the urethra and urinary bladder which, once the tissue can no longer distend, will result in pressure necrosis and mucosal injury. Pressure within the urinary bladder is then transmitted up the ureters to the kidneys with subsequent reduction of glomerular filtration. Within 24-48 hours of obstruction the kidney's excretory ability ceases, resulting in an accumulation of blood urea nitrogen, creatinine, phosphorus,

potassium, and hydrogen ions in the blood, which largely contributes to the clinical signs associated with UO.

Uremia can cause depression, nausea, vomiting and anorexia. The combination of decreased food and/or water intake and ongoing gastrointestinal losses from vomiting and diarrhea can result in dehydration and potential for hypovolemia. Severe hyperkalemia is considered to be the most life-threatening aspect of UO because of its effects on the cardiovascular system. Elevations in serum potassium affect electrical conduction through the heart by diminishing the rate of depolarization, resulting in bradycardia. If the serum potassium level gets high enough electrical activity in the heart can cease altogether, resulting in asystole. Severe metabolic acidosis can lead to denaturing of proteins, enzymatic dysfunction and catecholamine hyposensitivity.

Given these changes, it seems likely that hypotension and cardiovascular collapse could develop in the latter stages of urethral obstruction. However, a study assessing blood pressure at the time of presentation in 28 blocked cats, which included some animals with significant illness, found no incidence of hypotension (4). Instead it was found that more severely affected patients (having higher blood urea nitrogen, creatinine, and potassium concentrations) tended to be normotensive, whereas less severely affect patients tended to be hypertensive, suggesting that several factors (*e.g.*, pain, stress) may have served to offset any tendency towards hypotension.

History and clinical signs

The classic history associated with UO involves a male cat which has been vocalizing and straining unproductively in the litterbox. However, these signs may be difficult to distinguish from a cat with FIC. Ideally, determination of whether urine is produced can help decide if UO has occurred. Unfortunately, cats with cystitis will often urinate very small amounts frequently, and sometimes outside the litter box, making it difficult to know for sure if the cat is producing urine. In addition, multi-cat households can present a challenge for owners to keep track of whether or not the cat has been urinating.

One distinguishing feature of UO *versus* cystitis is that affected cats start to show signs of systemic illness as the obstruction progresses; this could include vomiting, lethargy, anorexia, and abdominal pain which progress to changes in mentation and lateral recumbency. These signs are fairly non-specific if UO is not suspected, so obstruction should be considered as a differential for any sick male cat!

Clinical signs can vary considerably depending on the stage at which the patient is presented. Cats that present early may not have any striking physical exam findings aside from a firm, distended urinary bladder. In the "healthy" blocked cat this is the most definitive method to distinguish between obstruction and cystitis (as cats with cystitis should have a small, barely palpable bladder). If the obstruction has been present for more than 24 hours the patient may show signs of systemic illness such as dehydration, bradycardia, and hypothermia.

The presence of bradycardia in male cats should always raise concern for hyperkalemia, as the normal stress response to hospital presentation should result in tachycardia (although cats in septic or cardiogenic shock can also demonstrate bradycardia). In fact, the combination of bradycardia (HR < 140) and hypothermia (< 96.6°F/36°C) has been found to be 98% predictive of serum potassium level greater than 8 mEq/L in cats with urethral obstruction (5).

Initial diagnostics and stabilization

Presentation of the "sick" blocked cat warrants immediate medical attention. An IV catheter should be placed and initial blood samples for packed cell volume (PCV), total protein (TP) and blood gas or chemistry panel (which should include glucose, urea and creatinine) obtained if possible. Fluid therapy should be started immediately to support vascular volume and help dilute the serum potassium concentration, even if bladder decompression cannot be performed immediately. There is some debate as to the optimal type of fluid to use. Traditionally, 0.9% NaCl has been considered the fluid of choice because it has a greater dilutional effect on potassium; however it is also an acidifying solution which may serve to exacerbate metabolic acidosis.Conversely, balanced electrolyte solutions are alkalinizing but contain small amounts of potassium (typically 4-5 mEq/L) which may have less of a dilutional effect. A recent study comparing 0.9% NaCl and a balanced electrolyte solution showed no difference in outcome parameters (survival, length of stay) or in reduction of serum potassium levels, although acid-base anomalies corrected more rapidly in the latter group (6).

Overall it seems that the fluid chosen does not matter as long as an adequate volume is administered. If cardiovascular

collapse is present it may be necessary to administer crystalloid "shock doses" (40-60 mL/kg) in bolus fractions (1/4-1/3 of the calculated shock dose over 15-20 minutes, repeated as necessary) to rapidly restore vascular volume and reverse signs of cardiovascular instability. If resuscitation is not necessary, fluid rate should be based on replacement of dehydration added to the maintenance fluid requirement. If time does not allow more accurate determination of fluid rate, it is reasonable to start at a rate of 10 mL/kg/h in the initial stages, provided there is no indication of underlying heart disease.

An ECG should be obtained (even if the patient is not demonstrating bradycardia) to determine any effects hyperkalemia might be having on electrical conduction in the heart. Classic ECG changes associated with hyperkalemia include prolonged P-R interval, diminished or absent P waves (1), widened QRS complexes (2) and tall, tented T waves (3) ***(Figure 1)***. As hyperkalemia worsens, ECG changes can progress to atrial standstill, ventricular fibrillation or asystole. While de-obstruction and IV fluids will ultimately be the primary means of eliminating potassium and reversing the adverse affects of hyperkalemia, this process takes time. If the patient has significantly bradycardia (HR < 140) then immediate intervention to protect the heart (using calcium gluconate) and to promote intracellular shift of potassium (by regular insulin, dextrose, and/or sodium bicarbonate) should be employed ***(Table 1)***.

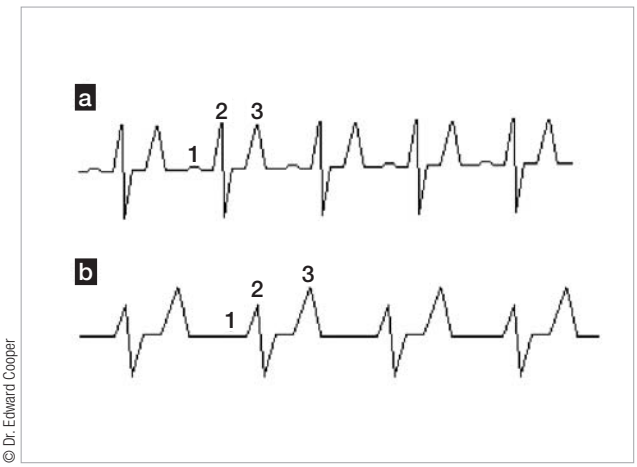
Given that calcium gluconate does not serve to decrease potassium levels, if it is administered the patient should also receive dextrose, or insulin and dextrose; note that dextrose should be given when insulin is administered to prevent the development of hypoglycemia.

Though controversial, cystocentesis can also be a part of initial stabilization by allowing immediate relief of pressure within the urinary tract and more rapid resumption of glomerular filtration. This could be especially important when a busy emergency department does not afford the time necessary to relieve the obstruction by passing a urinary catheter. In addition, only minimal sedation (or even no sedation) is usually necessary to perform cystocentesis (as opposed to heavy sedation/anesthesia for catheterization) and a "pure" urine sample can be obtained for urinalysis or urine culture. Finally, relieving the back-pressure against the obstruction (whether stone, plug or spasm) may make for easier passage of a urinary catheter. The major concern raised against performing cystocentesis in cats with urethral obstruction (UO) is the potential for tearing or rupture of a distended and friable bladder with resultant uroabdomen. A recent prospective study of 45 blocked cats demonstrated that development of clinically significant abdominal effusion, as evidenced by abdominal ultrasound, occurs rarely after cystocentesis and that this procedure can be safely performed (7).

Urethral catheterization

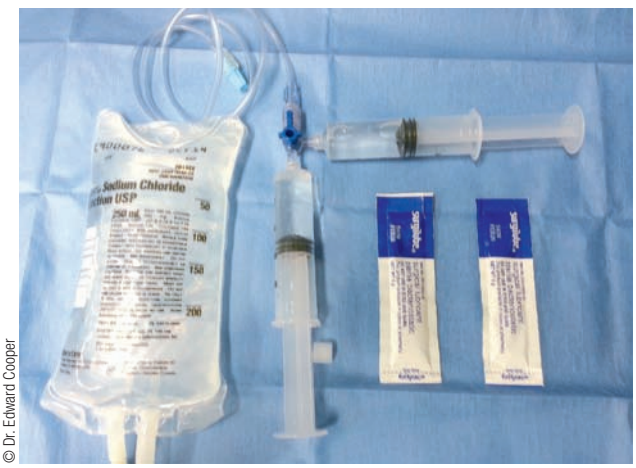
Passage of a urinary catheter to relieve a physical obstruction is generally considered to be essential in the management of UO. In order to optimize the likelihood of successful catheterization and minimize damage to the

Figure 1. Potential ECG changes associated with **(a)** moderate (approx. 6.0-8.0 mEq/L) and **(b)** severe (> 8.0 mEq/L) hyperkalemia.



© Dr. Edward Cooper

Figure 2. Catheter flushing apparatus, including two syringes, 3-way stopcock, extension tubing, sterile saline and sterile lubricant.



© Dr. Edward Cooper

Table 1. Emergency dose rates for severe hyperkalemia.

Medication	Dose (IV)	Rate of administration	When to administer
Isotonic crystalloid	10-15 mL/kg 10 mL/kg/hr	15-20 minutes Constant rate infusion	Shock Initial replacement fluid rate
Calcium gluconate	50-150 mg/kg	Over 5 minute period	Bradycardia, major ECG changes
Regular (soluble) insulin	1 unit	IV bolus	If Ca gluconate given Potassium > 8 mEq/L
50% dextrose	0.5 g/kg	Over 3-5 minute period	If Ca gluconate given Potassium > 8 mEq/L
Sodium bicarbonate	1 mEq/kg	Over 5 minute period	Potassium > 10 mEq/L

urethra, heavy sedation/analgesia or anesthesia is recommended ***(Table 2)***. Vocalization or movement during catheterization attempts, reflecting insufficient sedation, is likely to be associated with significant urethral spasm and an increased risk of urethral trauma. Under these circumstances higher doses or additional medications should be given. Once the patient is sedated/anesthetized, the perineal area should be clipped, prepared and draped in order to minimize risk of contamination. An open-ended semi-rigid catheter (polypropylene or polytetrafluoroethylene) can be used to initially relieve the obstruction. Creating a mixture of saline and sterile lubricant (in a ratio of 5:1) as the flush solution will serve to deposit lubricant along the entire length of the urethra and potentially decrease urethral damage ***(Figure 2)***. Another helpful technique is to pull the prepuce caudally once the catheter is seeded in the penile urethra ***(Figure 3)***. This will straighten out the urethra, thus making passage of the catheter easier and less traumatic. Once the initial catheter is in place the urinary bladder can be emptied and flushed. Given that a polypropylene catheter is rigid and can cause significant urethral irritation, it should be withdrawn and replaced by a softer indwelling catheter (typically 3.5 or 5 Fr) which is then sutured in place. It has recently been demonstrated that use of a 3.5 Fr urinary catheter may be associated with less risk of immediate re-obstruction when compared to a 5 Fr catheter (8).

Once the patient has been stabilized and the obstruction relieved, it is important to obtain abdominal radiographs (perhaps even a single lateral view) encompassing the entire lower urinary tract to assess catheter placement and to identify the presence of calculi, as management will differ if stones are present.

Post-obstructive care

Fluid therapy and monitoring urine output are important aspects of post-obstructive care. Patients which have had prolonged obstruction are at risk for a post-obstructive diuresis resulting in massive urine production. This diuresis is thought to occur secondary to the accumulation of osmotically active substances in the blood, pressure necrosis, medullary washout and/or anti-diuretic hormone resistance brought about during the obstructive process.

One study has demonstrated that this can occur in up to 46% of cats in the post-obstructive period (9). While severity of azotemia was not found to be associated with likelihood, blood pH did have a significant negative correlation. It is very important to keep up with urinary losses in these patients, as the cat can quickly become severely dehydrated and hypovolemic; do not fear the high fluid rates required to keep up with losses in these patients!

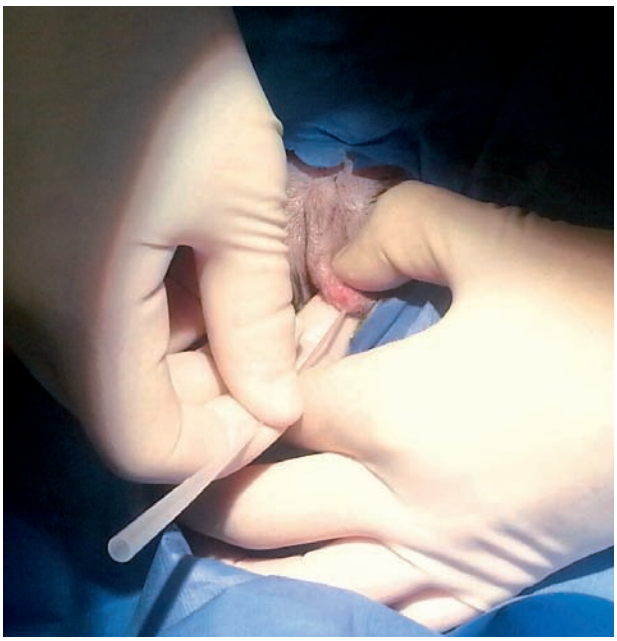
Another potential concern is for inadequate urine production (< 1mL/kg/hr) after the obstruction is relieved, which may occur as a result of obstruction in the collection system or dehydration. True oliguria can occur as a result of progression to acute renal failure, but this appears to be very uncommon in urethral obstruction.

Another important aspect of post-obstructive care is analgesia and sedation. Cystitis and obstruction, in addition to urethral catheterization, are painful and

could be associated with risk of re-obstruction. Buprenorphine (0.01-0.02 mg/kg q8H) generally provides sufficient pain control and has the benefit of transmucosal administration if desired. If buprenorphine is not sufficient, fentanyl (2-4 µg/kg/hr) as a continuous rate infusion (CRI) is recommended. Because of the potential to cause excitability and hyperthermia, hydromorphine is typically avoided. Acepromazine (0.05 mg/kg IV/IM or 0.5 mg/kg PO) can provide adequate sedation to decrease stress and agitation, so long as the patient is stable (*i.e.,* resolution of dehydration/hypovolemia). The α-antagonist effects of acepromazine might promote urethral relaxation and decrease the risk of re-obstruction once the urinary catheter is removed.

Another frequent consideration in the post-obstructive period is whether the patient should be given antibiotics. It has traditionally been accepted that the incidence of bacterial infection in feline lower urinary tract disease is very low (< 2%), but more recent studies have suggested a higher incidence, ranging from 25-40% (10,11). A recent prospective study, specifically in patients with feline urethral obstruction, found zero positive cultures at presentation, but 6/18 cats (33%) developed urinary tract infections while catheterized (12). However, another recently completed study of 31 cats also showed no positive cultures at presentation, and only 13% (4/31) went on to develop a positive culture (13). Given the low incidence, performing a urine culture and sensitivity at the time of catheter removal is recommended to determine if a urinary tract infection (UTI) has been introduced. As there is significant potential for contamination during catheter removal, the practice of submitting the catheter tip for culture should be avoided.

Electrolytes and renal values should be monitored every 12-24 hours and should rapidly correct to normal. Typically if there is not significant reduction in renal values within 24 hours, complications (*e.g.*, renal failure, uroabdomen) may have occurred. Hypokalemia can develop (especially in patients with post-obstructive diuresis) and potassium should be supplemented accordingly. The urinary catheter should remain in place until the cat is clinically improved, blood work has normalized, post-obstructive diuresis has resolved, and urine is free of major debris, clots or plugs in order to help minimize the risk of immediate re-obstruction. Note that a closed catheter system is preferred, although in some situations an open catheter may be used if there is concern that the patient will become entangled. Once the catheter has been removed



© Dr. Edward Cooper

Figure 3. Initial urinary catheter placement. The perineal region is firstly clipped, prepared and draped. Once the catheter is introduced into the distal urethra, the prepuce is pulled caudally to straighten the urethra and facilitate passage.

Table 2. Suggested anesthesia protocols when treating urethral obstruction.

Stable patient
• Premedication/sedation - Ketamine (5-10 mg/kg) + diazepam/midazolam (0.25-0.5 mg/kg) IV/IM or - Buprenorphine (0.01-0.02 mg/kg) and acepromazine (0.03-0.05 mg/kg) IV/IM • Induction - Propofol (1-4 mg/kg IV, to effect) • Maintenance - Inhalant anesthesia (isoflurane/sevoflurane)
Unstable patient*
• Sedation - Buprenorphine (0.01-0.02 mg/kg) + diazepam/midazolam (0.25-0.5 mg/kg) IV/IM or - Methadone (0.2-0.25 mg/kg) + diazepam/midazolam (0.25-0.5 mg/kg) IV/IM

*Typically general anesthesia is not only not required for very unstable cats (metabolically deranged, minimally responsive), it may have too much cardiovascular impact, and it is usually possible to unblock these patients under sedation alone.

the cat should be observed for 12-24 hours to ensure effective spontaneous urination prior to discharge.

Alternative management protocols

Unfortunately, the ability to provide the optimal treatment course outlined above may be limited by an owner's financial constraints. In addition, there is evidence that UO is as much a mechanical obstruction (urethral edema and spasm) as a physical one (plug or stone). A recent study demonstrated that pharmacological manipulation (analgesia and sedation), a low stress environment, and intermittent cystocentesis can result in spontaneous urination without the need for catheterization (14), the less invasive approach being offered in lieu of euthanasia when traditional treatment for UO was prohibited by financial constraints. Cats in need of emergency stabilization based on significant physical exam/metabolic derangements were excluded. Treatment involved administration of standardized doses of acepromazine and buprenorphine, decompressive cystocentesis, and subcutaneous fluids as necessary for up to four days. The cats were also placed in isolated housing with minimal handling to reduce stress associated with the hospital environment. The average cost of treatment was much lower than the cost for traditional UO management, and of 15 cats treated using this protocol a successful outcome (spontaneous urination and survival to discharge) was recorded in 11 (73%) cases. Major complications resulting in euthanasia included the development of uro-abdomen or hemo-abdomen, although there was no evidence of overt bladder tear/rupture on *postmortem* examination. Follow-up was performed at 3 days, 3 weeks, and 1 year after discharge; there did not appear to be a greater risk of immediate or long-term re-obstruction with this protocol when compared historically to traditional management.

These results suggest that this protocol could serve as an alternative to euthanasia based on financial constraints, but it cannot be recommended as an alternative to traditional management (which carries a reported success rate of 91-94%) as no direct comparison between the two has been made.

In some cases, financial limitations might preclude the ability to hospitalize for treatment. Under those circumstances it may be necessary to offer euthanasia, especially for severely affected cats (hypothermia, bradycardia, lateral recumbency, etc). For those patients presenting in the earlier stages of obstruction that are not yet significantly ill, it may be possible to provide care on an outpatient basis, though this should be reserved as a last resort. One option would be to provide sedation and analgesia (acepromazine and buprenorphine) and bladder decompression through either catheterization or cystocentesis. Catheterization would offer the benefit of removing any physical obstruction but could also result in urethral damage or irritation and an increased risk of re-obstruction. Cystocentesis would likely be less expensive to perform and less injurious to the urethra, but might only provide temporary relief if a physical obstruction is present.

With either approach, the patient would be discharged with recommendations as outlined below in the hopes that continued analgesia and sedation will allow for spontaneous urination to occur. Aside from anecdotal reports and clinical experience, there is no evidence to support the merits of either of these approaches, nor is there information regarding the likelihood of success or recurrence. The client would have to be well-informed of the potential for treatment failure and follow-up phone calls to determine response would be strongly recommended.

At-home care

Given the potential for recurrence, at-home care may be extremely important to help decrease the likelihood of re-obstruction either immediately or in the future. Continued analgesia and sedation after discharge can be helpful, with administration of acepromazine and buprenorphine for 5-7 days. For patients demonstrating significant straining/urethral spasm after catheter removal, it may also be beneficial to administer prazosin (0.25-0.5 mg q12-24H) as an α-1 antagonist and urethral relaxant. Antibiotics should only be dispensed based on results of urine culture taken at the time of catheter removal. Other recommendations which have been made to help decrease the risk of re-obstruction include increasing water intake by switching to wet food, flavoring the water, or using a running-water bowl.

Given the questionable role that urinary crystals play in the pathogenesis of obstruction, it is unclear whether dietary manipulation of urinary pH to address crystalluria is beneficial, but since stress may play a potential role in the pathogenesis of this disease, environmental enrichment may also help (15, 16).

Prognosis

Depending on the underlying cause, there is an approximately 25-40% incidence of recurrence with UO (2,11).

With a second obstructive episode it becomes more likely that there will be subsequent occurrences, at which point it may be necessary to consider perineal urethrostomy. This surgical procedure (which is outside the scope of this paper) can significantly decrease the likelihood of UO, but does not serve to resolve signs of underlying FIC. In addition, these patients may be at an increased risk for UTI, although a recent study of 86 cats that underwent perineal urethrostomy showed good long-term quality of life with minimal risk of recurrence (17).

References

1. Bartges JW, Finco DR, Polzin DJ, *et al*. Pathophysiology of urethral obstruction. *Vet Clin North Am Small Anim Pract* 1996;26(2):255-264.
2. Gerber B, Eichenberger S, and Reusch CE. Guarded long-term prognosis in male cats with urethral obstruction. *J Feline Med Surg* 2008;10:16-23.
3. Buffington CA, Teng B, Somogyi GT. Norepinephrine content and adrenoceptor function in the bladder of cats with feline idiopathic cystitis. *J Urol* 2002;167(4):1876-1880.
4. Malouin A, Milligan JA, Drobatz KJ. Assessment of blood pressure in cats presented with urethral obstruction. *J Vet Emerg Crit Care* 2007;17(1):15-21.
5. Lee JA and Drobatz KJ. Historical and physical parameters as predictors of severe hyperkalemia. *J Vet Emerg Crit Care* 2006;16(2):104-111.
6. Drobatz KJ, Cole SG. The influence of crystalloid type on acid-base and electrolyte status of cats with urethral obstruction. *J Vet Emerg Crit Care* 2008;18(4):355-361.
7. Cooper ES, Weder C, Butler A, *et al*. Incidence of abdominal effusion associated with decompressive cystocentesis in male cats with urethral obstruction. In *Proceedings,* 19th Annual Vet Emerg and Crit Care Symp 2013; 801.
8. Hetrick PF and Davidow EB. Initial treatment factors associated with feline urethral obstruction recurrence rate: 192 cases (2004-2010). *J Am Vet Med Assoc* 2013;243:512-519.
9. Francis BJ, Wells RJ, Rao S, *et al*. Retrospective study to characterize post-obstructive diuresis in cats with urethral obstruction. *J Feline Med Surg* 2010;12:606-608.
10. Eggertsdottir AV, Lund HS, Kronveit R, *et al*. Bacteriuria in cats with feline lower urinary tract disease: a clinical study of 134 cases in Norway. *J Feline Med Surg* 2007;9:458-465.
11. Segev G, Livne H, Ranen E, *et al*. Urethral obstruction in cats: predisposing factors, clinical, clinicopathological characteristics and prognosis. *J Feline Med Surg* 2011;13:101-108.
12. Hugonnard M, Chalvet-Monfray K, Dernis J, *et al*. Occurrence of bacteriuria in 18 catheterised cats with obstructive lower urinary tract disease: a pilot study. *J Feline Med Surg* 2013;15(10):843-848.
13. Cooper ES, Lasley E, Daniels J, *et al*. Incidence of urinary tract infection at presentation and after urinary catheterization in feline urethral obstruction. In *Proceedings*, 19th Annual Vet Emerg and Crit Care Symp 2013; 815.
14. Cooper ES, Owens TJ, Chew DJ, *et al*. Managing urethral obstruction in male cats without urethral catheterization. *J Am Vet Med Assoc* 2010; 237(11):1261-1266.
15. Buffington CAT, 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(4):261-268.
16. www.indoorcat.org
17. Ruda L and Heiene R. Short- and long-term outcome after perineal urethrostomy in 86 cats with feline lower urinary tract disease. *J Small Anim Pract* 2012;53(12):693-698.

Imaging the urinary tract

William Widmer, DVM, MS, Dipl. ACVR
College of Veterinary Medicine Purdue University, West Lafayette IN, USA

Dr. Widmer is a board-certified specialist in diagnostic imaging and presently maintains a private consultation service in Indiana. He is also Professor Emeritus in Veterinary Radiology at the Purdue University College of Veterinary Medicine, where he was a faculty member from 1988 through 2009. After graduation from the College of Veterinary Medicine at Purdue in 1969 he was in private practice for 15 years before returning to Purdue for a combined graduate program and radiology residency. A Master of Science degree was earned in 1986, residency was completed in 1987 and Diplomate status in the American College of Veterinary Radiology was attained in 1988.

Introduction

Conventional radiography and contrast procedures were the primary imaging methods for the urinary tract in veterinary patients during the 20th century, and whilst diagnostic ultrasound is currently used for evaluating many urinary conditions radiography still plays a very important role for diagnosis and case management; indeed radiography and ultrasound are complementary procedures and should be used together for evaluating veterinary patients with urinary signs. The main radiographic contrast procedure used for urinary tract disease is the excretory urogram (EU). Computed tomography (CT) competes well with radiology and ultrasound for evaluation of many urinary tract conditions, and magnetic resonance imaging (MRI) is also used, but has cost and availability limitations. This paper emphasizes the combined use of radiography and ultrasound evaluation for the most effective approach to such cases.

KEY POINTS

- **Radiography and ultrasound are complementary procedures for examination of the urinary tract; each technique provides unique information, but radiography alone may be sufficient in many cases.**
- **Radiography is an excellent screening tool to assess organ size, shape, opacity and location within the abdomen.**
- **Ultrasound allows the examination of internal architecture of the renal parenchyma, the collecting system and the urinary bladder.**
- **Practitioners can use these modalities in conjunction to refine differential diagnosis of urinary diseases.**

The advantages of urinary tract radiography include cost-effectiveness, short procedure time, widespread availability and its simple technology. The arrival of computer-friendly digital systems that offer superior image contrast as well as savings in imaging time (*i.e.,* short throughput) have renewed interest in veterinary radiography. Radiography is a good survey method and is valuable for assessing changes in organ size, shape, opacity and location within the abdominal cavity (1,2). Its importance and cost-effectiveness should not be overlooked.

Ultrasonography provides unique information regarding the internal architecture (echotexture) and structure of urinary organs (3-6) and Doppler ultrasound examination can be used to assess renal blood flow, providing functional information (7). With the exception of the excretory urogram, radiology offers little information on the internal structure and function of the kidney. Nevertheless, radiography is valuable because it adds topographical information, which is lacking with ultrasound examination. Diagnostic ultrasound is non-invasive, non-ionizing and obtains information at little or no risk to the patient. However, ultrasonography cannot replace physical examination, urinalysis and survey radiography.

Most veterinarians either have access to, or own, ultrasound equipment but unfortunately, the equipment is

often underutilized because many veterinarians may be inexperienced with ultrasonography technique, are unsure of its indications, or do not have time to use it. While ultrasound is technically more difficult than radiography, the urinary tract is a good place for new sonographers to start - when considering different organ systems, the urinary tract is one of the easiest to examine and one of the most rewarding to study.

Radiography for renal conditions

Size, shape and margination changes of the kidney are well seen with radiography. Kidneys are normally smoothly marginated; the canine kidney has a true "bean" shape while the feline kidney has an oval to round shape. Renal size can be approximated by comparing the length of each kidney to the length of the second lumbar vertebra (L2) on standard ventrodorsal projections (normal kidney length equates approximately to 3 x L2 in the dog and 2.5 x L2 in the cat) (1,2). However, renal length should not be used as strict criteria for determining whether or not a patient has renal disease.

Changes in renal size and shape are readily evaluated with survey and contrast radiography (1,2) and the differential diagnosis for abnormal renal size is given in ***Table 1***. It should be kept in mind that evaluation of renal size is subjective and that even when a particular condition may have the potential for causing renomegaly, increased renal size may not actually be present. The same is true for small kidneys; a kidney may not be smaller than normal when renal disease is present. In addition, renal size may be reduced without signs of renal disease, due to the functional reserve capacity of the kidneys. Therefore, evaluation of renal size is an insensitive indicator for the presence of renal disease. Shape changes are of limited value in differential diagnosis, as many conditions will alter the kidney shape; irregularly marginated kidneys (*e.g.,* "lumpy, bumpy" kidneys) can be due to infarcts, nodular disease, neoplasia or fibrosis associated with end stage disease. Smoothly marginated kidneys on the other hand can be seen with hydronephrosis and (in cats) peri-renal pseudocysts.

Table 1. Differentials for abnormal renal size (1).

Large kidneys	Small kidneys
Bilateral • Nephritis - Acute nephritis - Pyelonephritis • Discrete cell neoplasia • Parenchymal cystic diseases • Peri-renal pseudocysts (cats) • Feline infectious peritonitis **Unilateral** • Hydronephrosis • Compensatory hypertrophy • Primary renal neoplasia (other than lymphoma) • Peri-renal pseudocysts (cats) • Subcapsular abscess • Subcapsular hematoma	**Bilateral** • End stage renal diseases (chronic nephritis) • Familial renal disease - Renal hypoplasia - Renal dysplasia • Hypotension • Normalcy (cats) **Unilateral** • Atrophy • Chronic obstruction • Chronic renal disease (nephritis)

Excretory urography (formerly known as intravenous pyelography or intravenous urography) is valuable for evaluating the kidneys and the remainder of the urinary tract, especially the ureters (1). This special procedure is particularly useful when diagnostic ultrasound examination is not available, and practitioners are still encouraged to use excretory urography as many of its original indications remain appropriate. The technique involves administering ionic or non-ionic iodinated contrast medium and following its excretion by glomerular filtration with serial radiography. The excretory urogram is characterized by the nephrogram and the pyelogram, which relate to the opacification of the renal parenchyma and collecting system (pelvis, diverticula and ureters) ***(Figure 1)***. If ultrasound is not available, excretory urography is useful for confirming shape changes seen or suspected on survey radiographs and to evaluate the renal pelvis and ureters ***(Figure 2)***. Indications for excretory urography are given in ***Table 2*** and method, imaging sequence and dose of contrast medium are available in the current literature (1,2).

Ultrasonography for renal conditions

Indications for nephrosonography include: i) palpable anomalies of the kidneys or urinary bladder, ii) laboratory evidence (*e.g.,* CBC, serum chemistry determinations, and urinalysis) of renal disease, iii) hematuria, iv) poor visualization of the kidneys on survey radiographs, v) suspected urolithiasis on survey radiographs, and vi) post-traumatic conditions where renal damage is suspected (6). The resistive index (RI) can be calculated from Doppler interrogation of the renal arterial supply, quantifying renal blood flow for each kidney (7). For standard two-dimensional grayscale imaging kidneys are readily visualized with equipment using 5-7.5 MHz sector scan heads (transducers) ***(Figure 3)***.

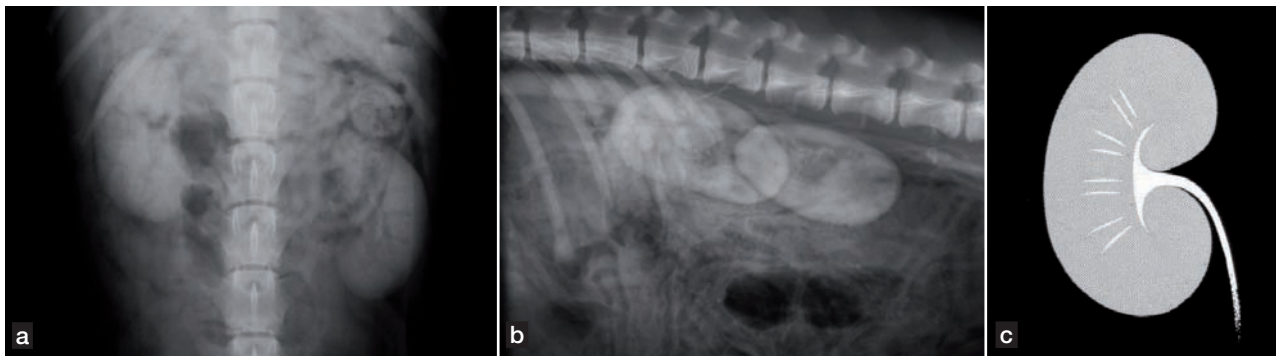


Figure 1. Normal excretory urography; ventrodorsal **(a)** and lateral **(b)** nephrogram phase demonstrates uniform opacification of the kidneys. Images were obtained immediately after injection of iodinated contrast medium, thus there is mild opacification of the surrounding viscera. **(c)** A pyelogram phase graphic illustrating normal filling of pelvis and renal diverticula on a ventrodorsal projection (thin, paired parallel lines radiating from the pelvis).

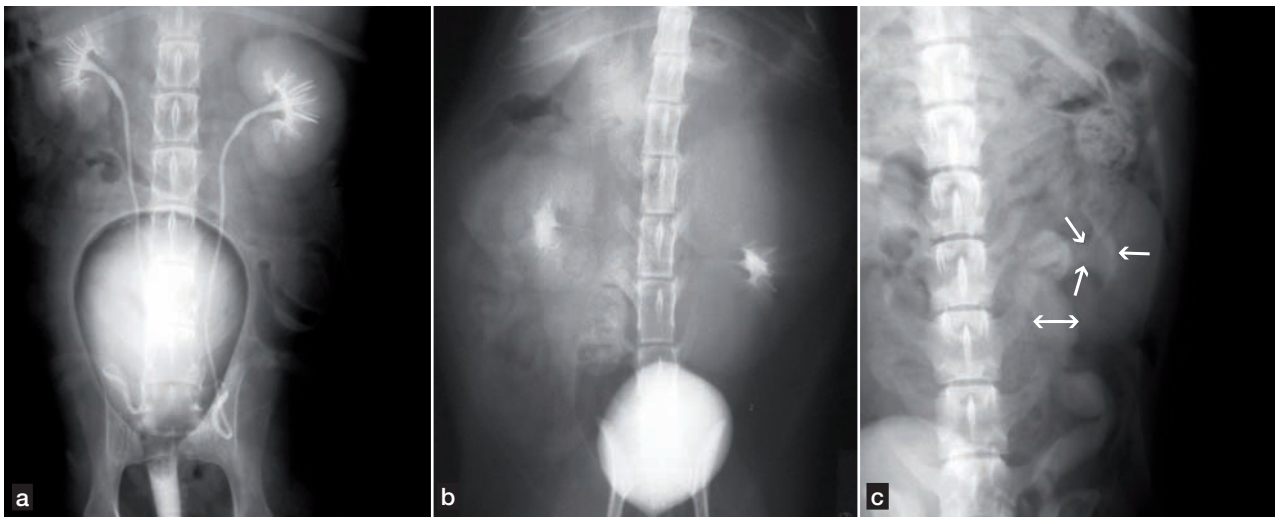


Figure 2. Abnormal excretory urography. **(a)** Pyelogram in a dog with mild pyelectasis; compare the size of pelvis and diverticula to those in ***Figure 1c***. Differentials for this degree of pyelectasia might include increased urine flow (polydipsia/polyuria), outflow obstruction, pyelonephritis and others. **(b)** Pyelogram of a cat with lymphoma. Note the altered shape of the kidneys and distortion of the renal pelvis and diverticula. **(c)** Pyelogram of a dog with ascending pyelonephritis; a megaureter is also present (double-headed arrow). In this patient, the renal diverticula are not visible due to swelling of the medulla, but the renal pelvis is dilated (arrows).

Normal kidneys have a well-demarcated cortex and medulla with the cortex being hyperechoic relative to the medulla ***(Figure 4)*** (4,6,7). The renal pelvis is usually not seen in normal animals but with high-resolution transducers it can occasionally be seen as a small anechoic linear stripe on sagittal orientation and as a "V" shape on transverse orientation (cross sectional images). The arcuate arteries are seen as hyperechoic foci near the corticomedullary junction and should not be confused with nephroliths. A hyperechoic area near the renal pelvis is a normal echo from fat in the renal sinus. The ureter is not seen in normal dogs and cats. Renal echogenicity is established by comparing the cortex to normal spleen or liver; the normal renal cortex is hypoechoic or iso-echoic to liver and hypoechoic to spleen. The renal medulla is hypoechoic to both organs. Relative echogenicity of the abdominal parenchymal organs is given in ***Table 3***.

Diffuse changes in renal echogenicity are common ***(Figure 5)*** (5-7). Hyperechoic kidneys may be associated with diffuse infiltrative diseases but the ultrasonographic appearance cannot predict histologic changes and will not provide a specific diagnosis; the individual cells that make up an infiltrative process cannot be resolved by sonography but changes in backscatter ("image noise") from the reflected ultrasound beam that differ from the normal appearance of the renal parenchyma

can be noted. In some instances, hyperechogenicity is due to replacement of normal cells and parenchymal organ components with scar tissue, which produces increased backscatter to the ultrasound transducer. Diffuse hyperechogenicity may be due to chronic nephritis (end stage renal disease), nephrocalcinosis, and some cases of lymphoma, but is also a normal aging change in both dogs and cats. Ethylene glycol toxicosis causes intense hyperechogenicity affecting the entire kidney due to deposition of calcium salts (8,9). Senior cats have a unique increase in renal cortical echogenicity due to lipid droplet deposition in the proximal convoluted tubules of the cortex (10); signs of renal disease do not accompany this condition, but lipid droplets may be shed in the urine, causing increased echogenicity of feline urine.

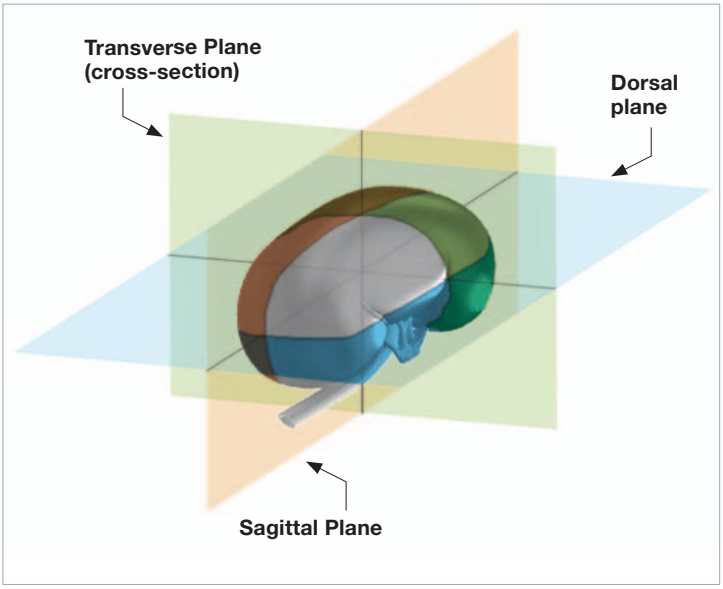


Figure 3. Ultrasound scan planes for examining the kidney. A sagittal plane splits the kidney lengthwise, into two equal halves. A transverse plane is a cross section made at 90^0 orientation to the sagittal plane. A third (dorsal) plane) is oriented 90^0 to the above. Sagittal and transverse plane images are superior to the dorsal plane for identifying structural changes in the kidney, especially for the collecting system (diverticula and pelvis). It should be kept in mind that the above description of image planes relates to the structure of the kidney and not orientation relative to the abdomen. Many publications use the orientation of the abdomen rather than the kidney, therefore, dorsal and sagittal may be substituted for each other.

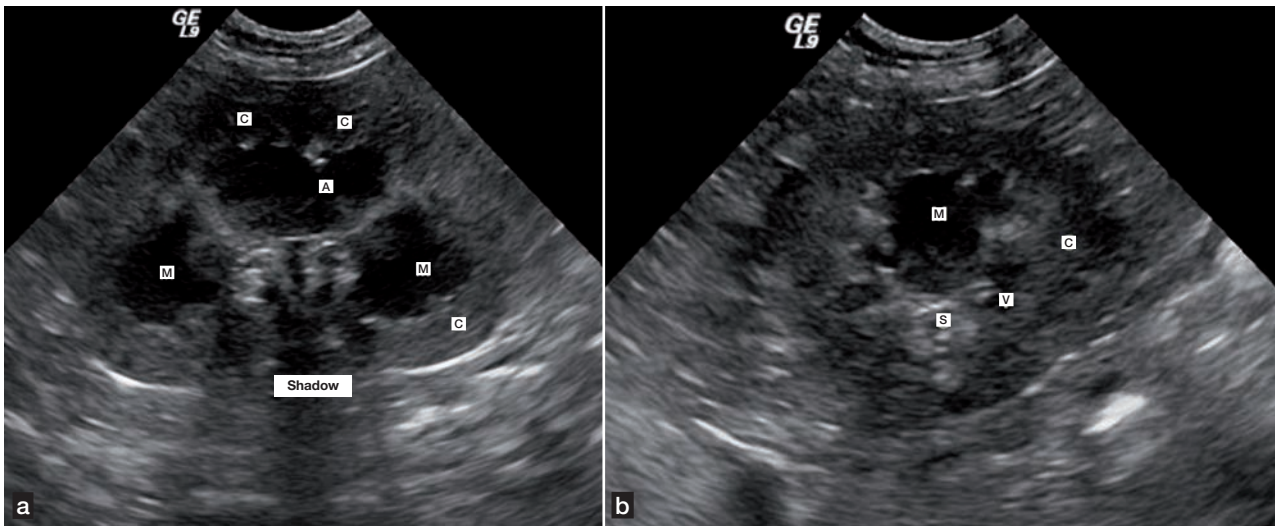
A 1-3 mm hyperechoic medullary band may be found near the corticomedullary junction in canine and feline kidneys (11). This is often due to previous insult to the region of the kidney occupied by the juxtamedullary nephrons, which is a watershed area of blood supply and oxygenation. Insults often result in mineralization and/or fibrosis, producing a “medullary rim sign”. Unfortunately this is not always a useful finding because it is often seen in animals without signs of renal disease or in animals recovered from a previous renal condition (12).

Hypoechoic kidneys are uncommon, but may be due to lymphoma, improper gain settings or poor transducer contact (7). With lymphoma, abnormal lymphoblastic infiltrates may displace normal parenchymal stroma, reducing the backscatter and hence echogenicity. Neonatal kidneys are often hypoechoic, especially the medullae, which may have less solute (osmolality is less, due to the underdeveloped concentrating mechanism). In addition extreme diuresis might also cause hypoechoic kidneys due to solute washout.

Shape change is best assessed with survey radiography or excretory urography, but can be detected with ultrasound examination (6). Irregular capsular margins can be seen with multiple infarcts, neoplasia, familial renal diseases such as polycystic kidneys and chronic nephritis, and in cats with feline coronavirus infection (7,13-15).

Table 2. Indications for excretory urography.

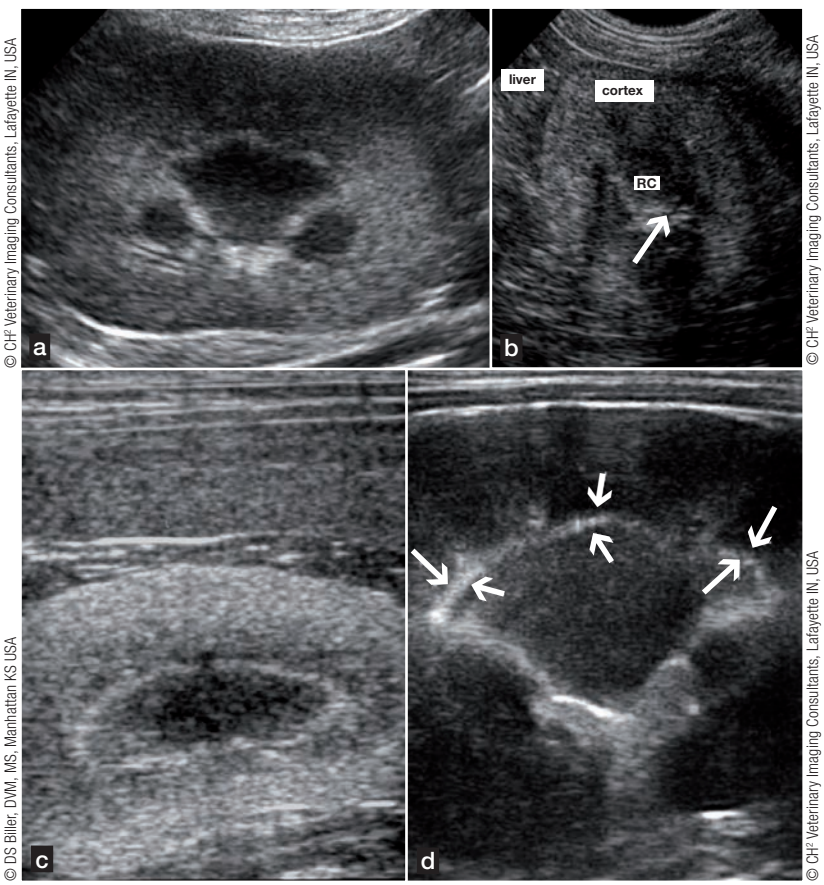
A nephrogram – where contrast delineates the renal parenchyma – is indicated in the following situations	A pyelogram – where contrast delineates the renal pelvis – is indicated in the following situations
• If the kidneys are poorly visualized on survey radiographs • For identification of opacification defects caused by tumors, infarcts and cystic changes • For assessment of glomerular function; the opacity and fading sequence of the nephrogram provides a very crude index of glomerular filtration rate (GFR)	• For identification of pyelectasis (renal pelvic dilation) • For detection of non-mineralized calculi and blood clots • For differential diagnosis when increased renal size is present to identify lack of filling of the diverticula (helping identify renal swelling seen in pyelonephritis and other conditions) • For visualization of the proximal aspect of the ureters



© Dr. William Widmer

Figure 4. Normal nephrosonograms. **(a)** Sagittal sonogram; the cortex (C) is hyperechoic to the medulla (M). An echo from arcuate artery (A) should not be confused with a urolith. The renal pelvis is not seen due to limited urine content; note the acoustic shadowing from the fat in the pelvic recess which is distal to the renal pelvis, which should not be confused with a nephrolith. **(b)** Transverse sonogram; the cortex (C) surrounds a hypoechoic medulla (M) and the renal sinus fat (S) is visualized distal to the pelvis (which is not seen). The two parallel lines are echoes from a renal vein (V).

Figure 5. Changes in renal echogenicity architecture and shape.
(a) Sagittal sonogram of a senior cat with no signs of urinary disease. The cortex is hyperechoic with respect to normal, most likely due to increased fat deposition in the renal tubular epithelium rather than nephritis.
(b) Transverse sonogram of a dog with signs of renal disease. There is loss of corticomedullary demarcation with increased echogenicity of the cortex and medulla, especially in the renal crest (RC). Note the echogenicity of the cortex is greater than the adjacent caudate lobe of the liver. There is slight dilation of the renal pelvis (the arrow depicts a thin anechoic line).
(c) Dorsal plane sonogram of a patient with ethylene glycol toxicosis. There is marked hyperechogenicity due to massive oxalate and hippurate crystal deposition throughout the cortex and medulla. This presentation may be also seen with lily toxicosis.
(d) A hyperechoic corticomedullary rim; note the hyperechoic band (arrowed) near the corticomedullary junction. This change is thought to be mineralization secondary to insult of the juxtamedullary nephrons. It may be seen in diseased as well as healthy cats and therefore has limited clinical significance.



© CH² Veterinary Imaging Consultants, Lafayette IN, USA
© CH² Veterinary Imaging Consultants, Lafayette IN, USA
© DS Biller, DVM, MS, Manhattan KS USA
© CH² Veterinary Imaging Consultants, Lafayette IN, USA

Focal renal changes are easily identified with ultrasound and classified as either solid or cyst-like (cystic) (6,7). Solid lesions consist of nodules, masses and infarcts. Nodules may be hyperechoic, isoechoic or hypoechoic with respect to surrounding parenchyma, and as with diffuse changes, the histologic type cannot be determined with ultrasound examination. Nodules may be due to primary or metastatic neoplasia, granuloma formation or (rarely) abscessation. Mass lesions are usually neoplastic and distort the normal kidney architecture. Infarcts vary in echogenicity depending on the stage of development; they may be wedge-shaped and often cause capsular depression.

Cyst-like lesions are anechoic, thin-walled and often produce small near-and-far echoes ("6 and 12 o'clock artifacts") due to their circular shape and liquid content ***(Figure 6)***. Cysts may occur with congenital disorders such as polycystic kidneys or may be secondary to chronic nephritis and loss of functional parenchymal tissue. Occasionally primary renal neoplasms might produce a cystic lesion, but a thin wall would not be expected in this situation. Cats can develop peri-renal pseudocysts that originate in the subcapsular space between the capsule and the surface of the cortex (16). These are apparent with ultrasound examination but cannot be differentiated from renomegaly on survey radiographs.

Ultrasound examination is useful for detecting renal pelvic and ureteral lesions (17,18) and has reduced the use of excretory urography in veterinary patients. Pyelectasis (pyelectasia) refers to dilation of the renal pelvis and diverticula; with ultrasound examination anechoic urine is seen in the pelvis, best seen in either sagittal or transverse orientation ***(Figure 7a)***. Causes of pyelectasis include intravenous fluid administration, polydipsia/polyuria, ureteral obstruction or ureteral sepsis (6,7,18). However, pyelonephritis is difficult to identify with ultrasonography; in acute pyelonephritis no ultrasonographic anomalies might be found other than slight renomegaly and mild renal pelvic dilation (7). In experimentally-induced canine pyelonephritis (19,20) a hypoechoic line was described in the mucosa of the renal pelvis; however, this may be time-course dependent and not always found in spontaneous cases. With chronic pyelonephritis, mild to moderate dilation of the renal pelvis is present, the renal pelvis and diverticula may be distorted and blunted, and focal increased echogenic areas may be seen in the medulla. In addition, urine may contain focal echogenicities from inflammatory cells. The proximal aspect of the ureter is frequently dilated when pyelonephritis is present due to bacterial endotoxin release (7). Differentiation of pyelectasis due to pyelonephritis *versus* hydronephrosis ***(Figure 7b)*** is aided by identifying inflammatory debris, blood clots and possibly small amounts of gas from bacterial sepsis (21).

Table 3. Relative echogenicity of abdominal parenchymal organs.

HYPOECHOIC ◄——► HYPERECHOIC
Ovary < renal medulla < renal cortex < liver < spleen < prostate < depot fat*

*Falciform fat is isoechoic to liver, an exception.

Non-mineralized as well as mineralized calculi can be seen with ultrasound, an advantage over radiography ***(Figure 7c)***. This is because calculi produce an acoustic interface whether or not they have sufficient mineral content to be seen radiographically, producing a strong acoustic shadow on ultrasound. Nephrolithiasis is confirmed by observing intense specular echoes from the renal pelvis or with acoustic shadowing. Calculi in the diverticula are more difficult to identify and may be confused with echoes from the arcuate arteries near the corticomedullary junction. Identification is maximized when high frequency transducers are used and the calculi are within the focal zone and/or large in size (6).

Renal parenchymal mineralization (nephrocalcinosis) may also cause focal hyperechoic areas and acoustic shadowing, but echoes originate from the parenchyma, not the renal pelvis and the degree of acoustic shadowing may be less intense. As mentioned previously, fat in the renal sinus is echogenic, but often the degree of acoustic shadowing is less than with calculi. Renal blood clots have mixed echotexture and do not cause shadowing.

Radiography for urinary bladder conditions

Survey radiography is a valuable screening method for assessing diseases of the urinary bladder and adjacent structures ***(Figure 8)*** (2, 22). It is frequently used to identify mineralizations of the urinary bladder; causes include calculi and dystrophic mineralization (23, 24) but note that only calculi with sufficient mineral content and size will be seen on survey radiographs. The urinary bladder is subject to displacements, which can give clues to enlargement of the prostate and uterus, perineal hernias and

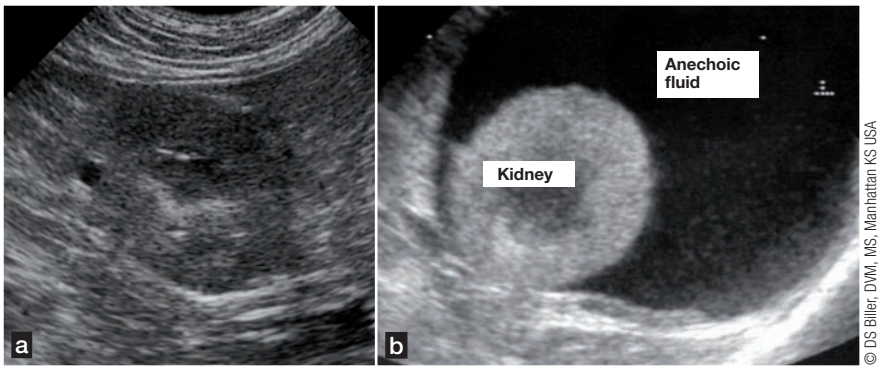


Figure 6. Cyst-like changes. **(a)** Sonogram of dog with chronic interstitial nephritis; a small anechoic cyst-like lesion can be seen in the periphery of the cortex. These lesions are usually insignificant unless they are diffuse, causing decreased functional renal mass *e.g.* as in polycystic renal diseases. **(b)** Peri-renal pseudocyst in a cat with azotemia; anechoic fluid lies within the subcapsular space and causes far enhancement of the renal parenchyma. On radiography this kidney would appear large, but the fluid would not be distinguished from the renal parenchyma.

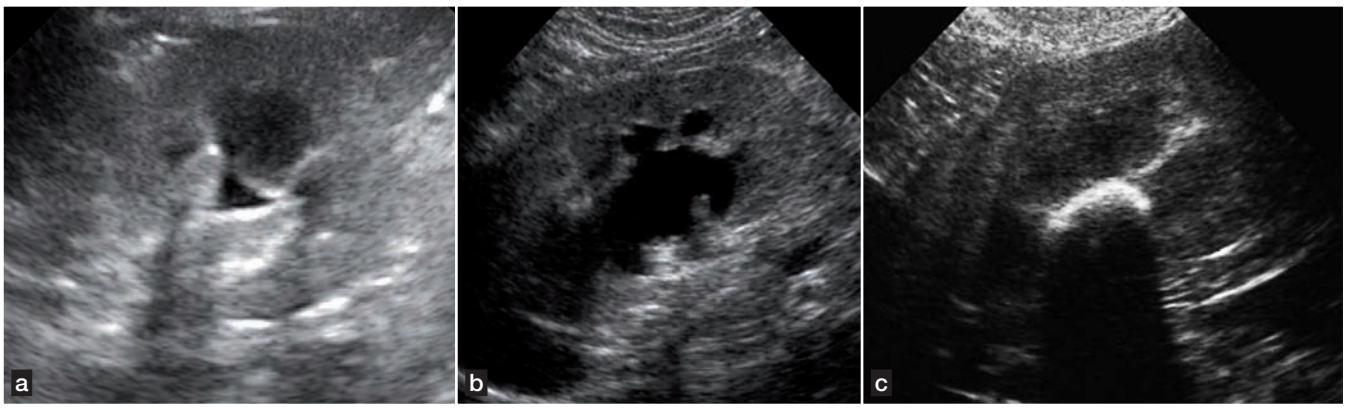


Figure 7. Renal pelvic lesions. **(a)** Transverse sonogram showing mild pyelectasis in a dog with polydipsia/polyuria due to renal failure. The triangular-shaped, dilated renal pelvis is best seen in this scan plane and contains anechoic urine. Note the hyperechoic medulla and loss of corticomedullary demarcation associated with renal disease. **(b)** Sagittal sonogram in a dog with hydronephrosis depicting marked dilation of the renal pelvis and diverticula with anechoic urine. **(c)** Sagittal sonogram of a canine kidney with a renal pelvic urolith. A bright specular curvilinear echo is present and a dark band is seen distal to the pelvis due to reflection and absorption of the ultrasound beam by the calculus.

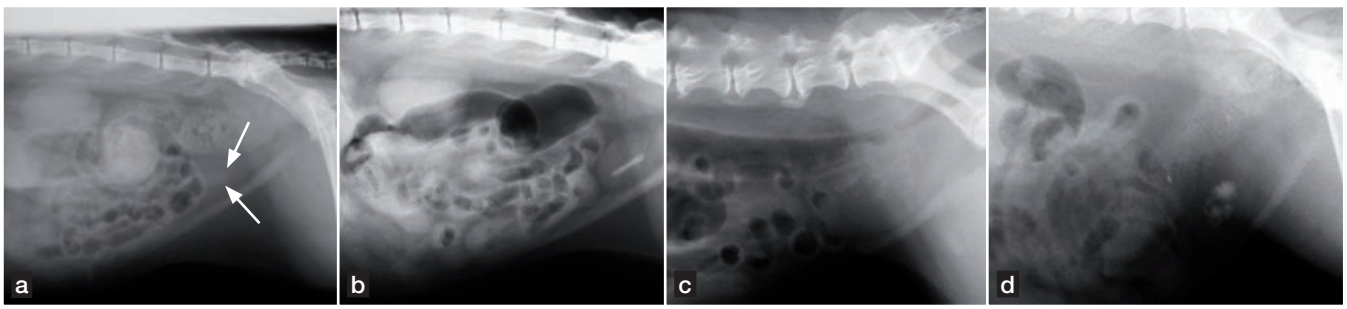


Figure 8. (a) Survey lateral abdominal radiograph of a cat with hematuria. A full colon compromises the study, but a mineralization is suspected in the vertex of the bladder (arrows). **(b)** Repeat radiography after an enema confirmed the presence of a urocystolith. Fasting and an enema should always precede radiography of the lower urinary tract; otherwise calculi and other changes may be inapparent. **(c)** Lateral radiograph of a dog with hematuria unresponsive to antibacterial therapy; faint, ill-defined wispy mineralizations are seen in the urinary bladder shadow. Ultrasound examination confirmed a mineralized mass at the junction of the trigone and body (see ***Figure 12a***). **(d)** Calcium oxalate and struvite uroliths have sufficient mineral content to be recognized on technically correct survey radiographs. This dog has calcium oxalate uroliths within its bladder.

sublumbar masses (22). Poor technique, non-distention or summation from overlying structures can cause non-visualization of the normal urinary bladder. Note that, contrary to popular opinion, the urinary bladder can often be seen when it is ruptured. Diseases affecting the urinary bladder wall such as cystitis, most neoplasms and congenital anomalies are not evident on survey radiographic studies.

Contrast radiography is a valuable follow-up to survey radiography, especially when ultrasound is not available (2,22,24). Cystographic procedures include pneumocystography, positive contrast cystography and double contrast cystography, and the specific techniques are well-documented (2, 22,24). Cystography allows visualization of the bladder wall, helping identify mural conditions such as cystitis and neoplasia, and filling defects caused by non-mineralized calculi, blood clots, neoplasms, and congenital defects such as ureterocoele ***(Figure 9)***. The chief use of positive contrast cystography is to detect urine leakage from the excretory pathway ***(Figure 9c)***. Cystography is also used with suspected prostatic disease to help locate and define the prostate, often with the aid of a urethrocystogram which allows visualization of the prostatic urethra.

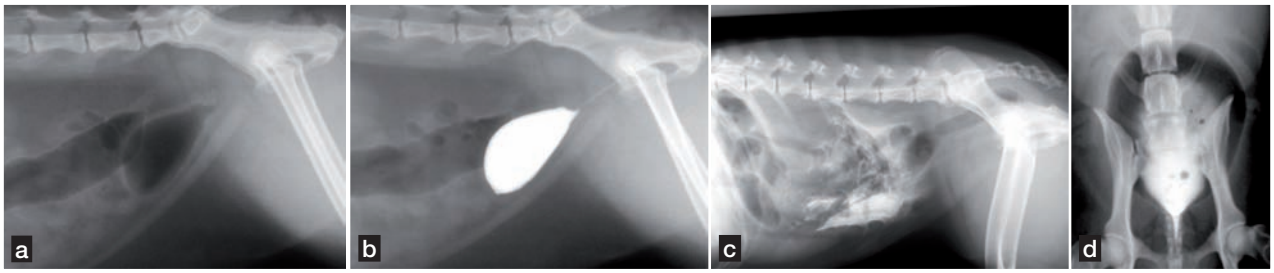


Figure 9. Contrast radiography of the urinary bladder. **(a)** Lateral pneumocystogram (negative contrast study) of a cat with chronic hematuria; a small mass can be seen at the dorsal aspect of the trigone. **(b)** Follow-up positive contrast cystogram of the same patient confirmed a mass in the trigone; a transitional cell carcinoma was diagnosed. **(c)** Positive contrast cystogram of a dog recently struck by a car; note the absence of a urinary bladder shadow and the presence of positive contrast medium in the peritoneal space. The ruptured urinary bladder was repaired surgically. **(d)** Double contrast ventrodorsal cystogram (pneumocystogram followed by administration of low volume of positive contrast medium) of a dog with crystalluria. Small circular filling defects (radiolucent areas) are seen in the dependent area of the urinary bladder where positive contrast medium has accumulated due to the effects of gravity. Note that four views will maximize the diagnostic yield: left lateral, right lateral, ventrodorsal and dorsoventral projections.

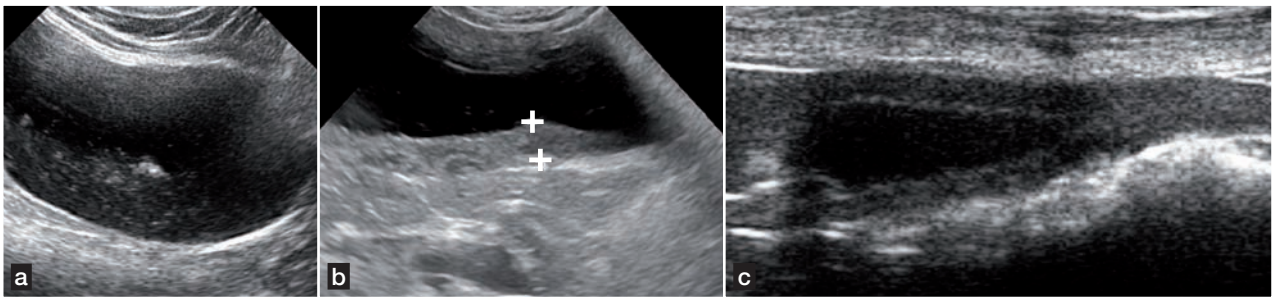


Figure 10. The urinary bladder is well-suited to ultrasound evaluation. **(a)** Normal sonogram, transverse plane, of a full urinary bladder in a cat. The distended bladder has a thin (~1 mm) wall and the lumen contains fine suspended echogenic debris, most likely due to fat particles - a normal finding in senior cats. **(b)** Partially filled urinary bladder, dorsal plane sonogram; the trigone is to the right of the image. The wall is thicker than in **(a)** because the bladder is less distended. The thickened area between the cursors is a papilla (vesicoureteral junction) and should not be confused with a mural lesion. Echogenic foci within the lumen near the papilla are a result of a ureteral "jet", indicating normal ureteral flow. However, this finding is inconsistent and cannot always be demonstrated. **(c)** Near-empty feline urinary bladder, dorsal plane sonogram. There is pseudothickening of the non-distended bladder due to folding of the mucosa and collapse of the remaining layers. An empty urinary bladder cannot be evaluated for mural lesions or wall thickness.

Ultrasonography for urinary bladder conditions

The urinary bladder is well-suited to ultrasound evaluation because of its fluid content, thin wall and caudal location within the abdomen ***(Figure 10)*** (6,23,24,25). In addition, because ultrasound examination is non-invasive and rapid, it is often used as a substitute for cystography. The urinary bladder should be examined in multiple planes (transverse and either dorsal or sagittal) to ensure lesions are not overlooked. The thickness of the normal urinary bladder varies with distention, appearing falsely thickened as it becomes empty, and so therefore should not be judged for thickness unless it is filled with urine; the same principle applies to cystography. A distended urinary bladder has regular thickness throughout (except for the vesicoureteral junction), usually 1-2 mm depending on degree of distention and body weight.

Ultrasound examination is often employed to search for cystic calculi, because most calculi produce a strong specular reflection and acoustic shadowing, even if they are small and have minimal mineral content ***(Figure 11)***. However, ultrasound is not reliable for measuring the

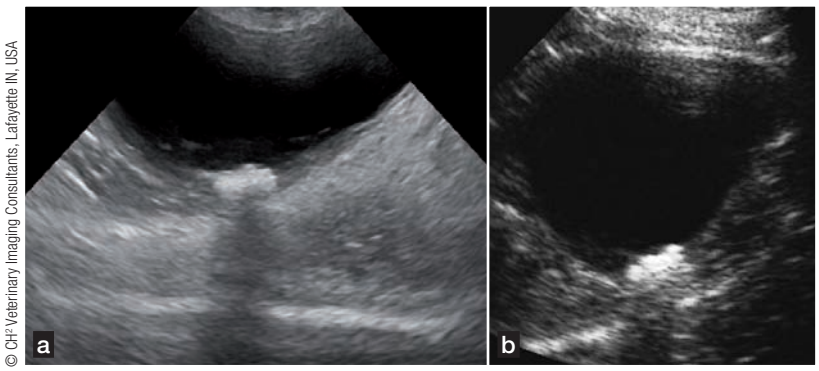


Figure 11. Ultrasound examination is often employed to search for cystic calculi. **(a)** Multiple urocystoliths in a dog; the calculi are small and have pooled, causing a strong reflection that misrepresents the size and number of calculi. Numerous small calculi were found at cystotomy. **(b)** Multiple urocystoliths in a cat. Small calculi are present, but many are separated, giving individual reflections. However, ultrasound should not be used to count number of calculi or to estimate size.

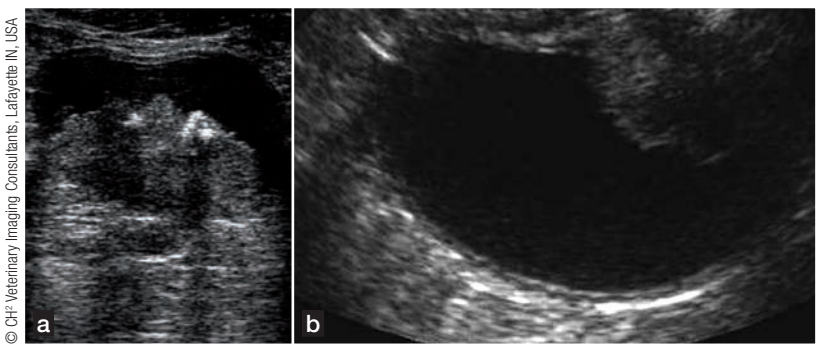


Figure 12. Ultrasound may be used to demonstrate urinary bladder masses. **(a)** Transverse plane sonogram of the mineralized bladder mass in the dog in ***Figure 8c***. The mass originates from the mucosa of the body of the bladder wall and the mineral within causes acoustic shadowing (the black vertical band in far field). **(b)** Dorsal plane sonogram of a dog with a dorsal trigonal non-mineralized bladder mass. This is a common location for a transitional cell carcinoma.

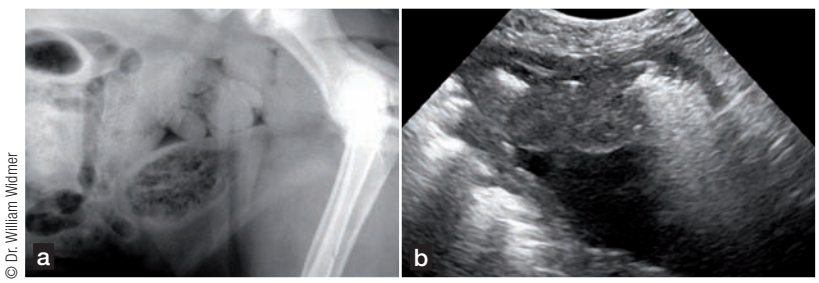


Figure 13. Emphysematous cystitis in a diabetic dog. **(a)** Lateral abdominal radiograph showing the urinary bladder with focal and linear gas opacities providing negative contrast due to a gas-producing bacterial infection. **(b)** Sonogram of the same patient demonstrating thickening of the bladder wall (near field wall); echogenic areas with comet tail/reverberation artifacts are visible, originating from gas within the wall of the bladder.

size, determining the shape, or counting the number of calculi present.

Wall thickenings due to cystitis or masses ***(Figure 12)*** and anomalies of the vesicoureteral junction can be seen with high-resolution equipment, a full bladder and judicious technique. However, rupture of the urinary bladder is rarely detected unless a large tear is present.

In many cases of cystitis, the urinary bladder wall is not thickened and will not appear abnormal on ultrasound examination, as the resolution is not sufficient to visualize small changes in the mucosa that might be seen with cystoscopy. An exception would be diffuse thickening due to chronic cystitis or changes produced by emphysematous cystitis ***(Figure 13)***.

Summary

In conclusion, the clinician is reminded that radiography of the urinary tract is useful for small animals because it can refine differential diagnosis and is cost-effective. It is an excellent screening method and should precede ultrasound examination. Ultrasound complements radiography because it adds information that cannot otherwise be obtained.

References

1. Seiler G. The Kidneys and Ureters. In: Thrall DE, ed *Textbook of Veterinary Diagnostic Radiography*, 6th ed, St Louis: Elsevier, 2013:705-725.
2. Johnston GR, Walter PA, Feeney DA. Diagnostic imaging of the urinary tract. In: Osborne CA, Finco DR. *Canine and Feline Nephrology and Urology*, Baltimore: Williams & Wilkins 1995: 230-276.
3. Nyland TG, Park RD, Lattimer JC, *et al.* Gray-scale ultrasonography of the canine abdomen. *Vet Radiol* 1981;21:220-227.
4. Konde LJ. Renal ultrasonography. *Vet Clin North Am Small Anim Pract* 1985;15:1149-1158.
5. Konde LJ, Park RD, Wrigley RH, *et al.* Comparison of radiology and ultrasonography in the evaluation of renal lesions in the dog. *J Am Vet Med Assoc* 1986;188:1420-1425.
6. Widmer WR, Biller DS, Adams LG, Ultrasonography of the urinary tract of the small animal patient. *J Am Vet Med Assoc* 2004;225:46-54.
7. Nyland TG, Mattoon JS, Hergesell, EJ, *et al.* In: *Small Animal Diagnostic Ultrasound*, 2nd ed, Nyland TG, Mattoon JS eds, Philadelphia, WB Saunders Company, 2002;158-195.
8. Adams WH, Toal RL, Breider MA. Ultrasonographic findings in dogs and cats with oxalate nephrosis attributable to ethylene glycol intoxication: 15 cases (1984–1988). *J Am Vet Med Assoc* 1991;199:492-496.
9. Adams WH, Toal RL, Walker MA, *et al.* Early renal ultrasonographic findings in dogs with experimentally induced ethylene glycol nephrosis in 1989. *Am J Vet Res* 1989;50:1370-1376.
10. Yeager AE, Anderson WI. Study of association between histologic features and echogenicity of architecturally normal cat kidneys. *Am J Vet Res* 1989;50:860-863.
11. Biller DS, Bradley GA, Partington BP. Renal medullary rim sign: ultrasonographic evidence of renal disease. *Vet Radiol Ultra* 1992;33:286-290.
12. Mantis P, Lamb CR. Most dogs with medullary rim sign on ultrasonography have no demonstrable renal dysfunction. *Vet Radiol Ultra* 2000;41:164-166.
13. Konde LJ, Wrigley RH, Park RD, *et al.* Sonographic appearance of renal neoplasia in the dog. *Vet Radiol* 1985:26:74-81.
14. Biller DS, Schenkman DI, Bortnowski H. Ultrasonic appearance of renal infarcts in a dog. *J Am Anim Hosp Assoc* 1991;27:370-372.
15. Biller DS, Chew DJ, DiBartola SP. Polycystic kidney disease in a family of Persian cats. *J Am Vet Med Assoc* 1990;196:1288-1290.
16. Beck JA, Bellenger CR, Lamb WA, *et al.* Perirenal pseudocysts in 26 cats. *Aust Vet J* 2000;78:166-171.
17. Felki C, Voros Fenyves B. Lesions of the renal pelvis and proximal ureter in various nephro-urological conditions: an ultrasonographic study. *Vet Radiol* 1995;36:397-401.
18. D'Anjou MA, Bedard A, Dunn ME. Clinical significance of renal pelvic dilation in dogs and cats. *Vet Radiol Ultra* 2001;52:88-94.
19. Neuwirth L, MaHaffey M, Crowell W, *et al.* Comparison of excretory urography and ultrasonography for detection of experimentally induced pyelonephritis in dogs. *Am J Vet Res* 1993;54:660-669.
20. Neuwirth L, Kuperus JH, Calderwoodmays M, *et al.* Comparative study of indium-111 leukocytes and nephrosonography for detection of experimental pyelonephritis in dogs. *Vet Radiol Ultra* 1995;36:253-258.
21. Choi J, Jang J, Choi H. Ultrasound features of pyonephrosis in dogs. *Vet Radiol Ultra* 2010;51:548-533.
22. Marolf AJ, Park RD. The Urinary Bladder. In: Thrall DE, ed Textbook of Veterinary Diagnostic Radiography, 6th ed, St Louis: Elsevier, 2013:726-743.
23. Weichselbaum RC, Feeney DA, Jessen CR, *et al.* An integrated epidemiologic and radiographic algorithm for canine urocystolith mineral type prediction. *Vet Radiol Ultra* 2001;42:311-319.
24. Johnston GR, Walter PA, Feeney DF. Radiographic and ultrasonographic features of uroliths and other urinary tract filling defects. *Vet Clin North Am Small Anim Pract* 1986;16:261-293.
25. Léveillé R. Ultrasonography of urinary bladder disorders. *Vet Clin North Am Small Anim Pract* 1998;28:799-821.

CUT-OUT AND KEEP GUIDE...

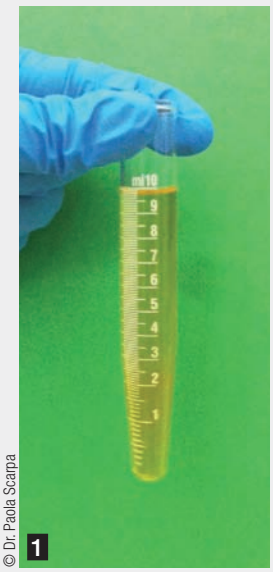
Urinalysis

Paola Scarpa, Prof. Dr. Vet., PhD.
Department of Veterinary Sciences and Public Health, Milan, Italy

Urinalysis is not only essential when investigating urinary disease, it can also be necessary for the diagnosis and monitoring of many systemic disorders. The possibility that poor protocol standardization can lead to inaccuracies in the analysis should not be underestimated. In addition, only a standardized method allows valid comparison of results obtained from different specimens (either between patients or serial specimens from the same patient).

1) Choice of tube

Tubes should be translucent (to allow the sample to be assessed for color and turbidity) and graduated to determine the exact volume of urine. Sterile tubes are preferred. In addition, urinalysis tubes are often conical to allow decanting of supernatant after centrifugation ***(Figure 1)*** but a round-bottomed tube may be considered as an alternative for easy re-suspension of the sediment.



© Dr. Paola Scarpa 1

2) USG

Use a refractometer to measure urine specific gravity (USG); remember that USG obtained by a dipstick is unreliable. Place two drops of urine onto the surface of the prism, close the cover plate and hold the refractometer towards the light to read the USG value ***(Figure 2)***.

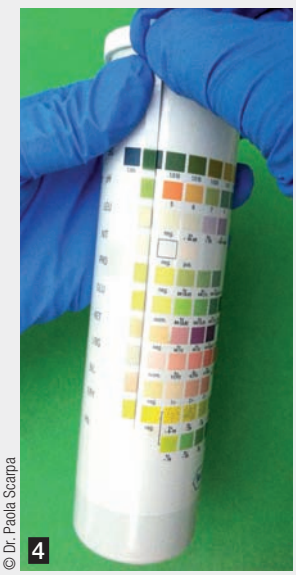

© Dr. Paola Scarpa 2

3) Dipstick

Before undertaking chemical examination by dipstick check the expiry date of the strips. A homogeneous specimen is essential to perform a correct analysis, so mix immediately before inserting the dipstick. Dip the test strip briefly into the urine, making sure that all test areas are moistened ***(Figure 3)***. Remove the excess urine, wipe the edge against the rim of the tube and dab the long edge of the strip on absorbent paper.


© Dr. Paola Scarpa 3

Compare the test areas with the colors on the packing vial under good lighting ***(Figure 4)***, at the exact time indicated by the manufacturer; use of a timer can be helpful. Accurate results will not be obtained at a later time-point, so avoid any other activity during the dipstick examination.


© Dr. Paola Scarpa 4

PITFALLS WHEN MANAGING URINE SAMPLES AND PERFORMING DIPSTICK TESTING

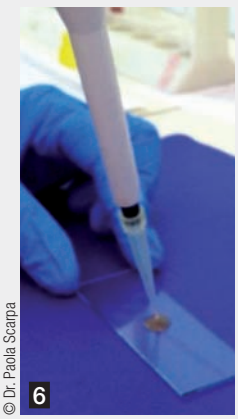
- **The leucocyte test gives unreliable results in dogs and cats: in cats a lack of specificity means that almost all urine samples give a false positive reaction. In dogs a lack of sensitivity gives false negative results. Evaluation for WBC in the urine should always be confirmed by microscopy.**
- **The blood test detects the heme group of compounds, so a positive result may be obtained because of hemoglobinuria, hematuria or myoglobinuria. Remember that erythrocytes tend to lyse in unconcentrated (USG < 1.015) or very alkaline urine.**
- **The nitrite test should not be used as an indicator of urinary tract infections because of its low sensitivity. In addition, the urgency of micturition associated with acute UTI may not allow enough time for bacterial reduction of nitrates (which takes typically 4+ hours).**
- **Calcium oxalate and struvite crystals can increase in number and size if urine samples are subject to excessive storage time and/or refrigeration.**

4) Sediment analysis

For a reliable result always use a defined volume of urine (usually 5 or 10 mL). Centrifuge the specimen at 400G or 1500-2000 rpm for 5 minutes; avoid a refrigerated centrifuge which can cause precipitation of crystals. Remove the supernatant with a pipette. If possible, do not decant: this is an inaccurate method that may also cause loss of cells.


© Dr. Paola Scarpa 5

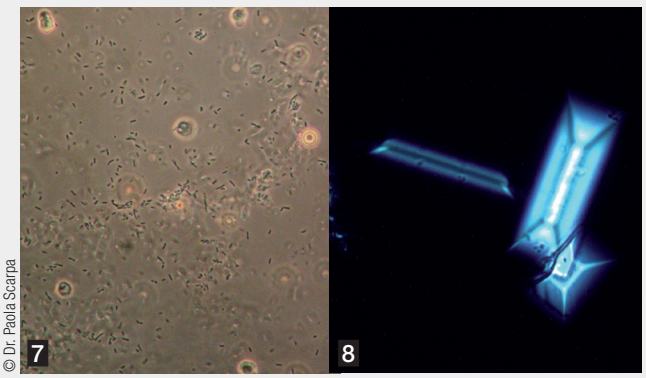
After removing the supernatant by suction ***(Figure 5)***, resuspend the sediment by gently mixing the remaining sample and transfer a known volume of sediment onto a microscope slide by pipette ***(Figure 6)***. Add the coverslip horizontally to maximize even distribution. The aliquot volume should be appropriate for the coverslip size: 13 µL for an 18 x 18 mm coverslip and 50 µL for a 24 x 32 mm coverslip.

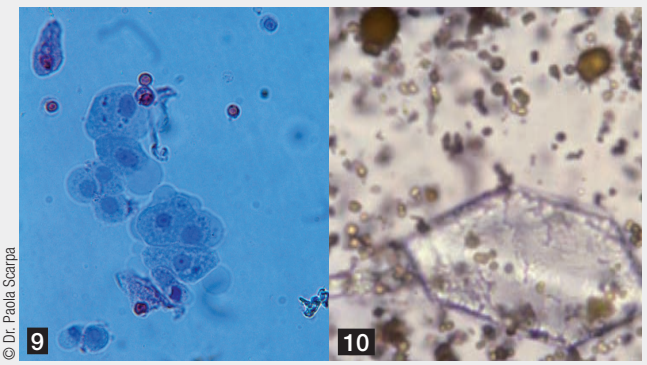

© Dr. Paola Scarpa 6

5) Microscopy phase

Contrast microscopy is preferred to bright-field microscopy, as it has much greater sensitivity for bacteria, hyaline casts and erythrocytes with low-hemoglobin content ("ghost cells"). It allows the best assessment of morphological details, an important feature for differentiation of cells or bacteria ***(Figure 7)***. Polarized light is useful to identify crystals and, in some cases, lipids ***(Figure 8)***. With bright-field microscopy, supravital stains (*e.g.,* Sternheimer-Malbin) are recommended to allow a better differentiation of cells, using a measure equivalent to 10% of the sample volume (*e.g.,* 50 µL of stain added to 0.5 mL of re-suspended sediment) ***(Figure 9)***. In bright-field struvite, calcium oxalate and cystine crystals appear colourless, while purine crystals appear brownish ***(Figure 10)***.

Examine the sample first under a low-power field (LPF), *e.g.* x 100; this allows visualisation of the particles on the slide, and for rare elements (casts, epithelial cells, crystals) to be identified. Then count the number of different particles visible under a high-power field (HPF), *e.g.* x 400, and obtain the average number of cells observed in at least 10 different high-power fields (use a low-power field if looking for casts) chosen from all areas under the coverslip.


© Dr. Paola Scarpa 7 8


© Dr. Paola Scarpa 9 10

SAVE THE DATE

24th ECVIM-CA CONGRESS

4th-6th September 2014

MAINZ | GERMANY

WWW.ECVIMCONGRESS.ORG

ROYAL CANIN

PLATINUM SPONSOR

5-year commitment to the ECVIM-CA congress

CONGRESS OF THE EUROPEAN COLLEGE OF VETERINARY INTERNAL MEDICINE - COMPANION ANIMALS