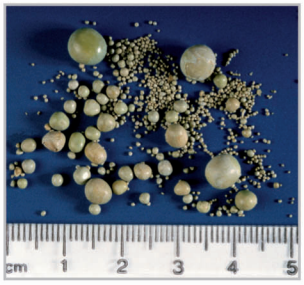
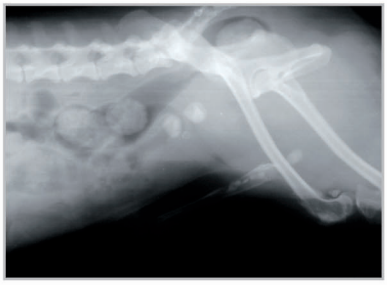
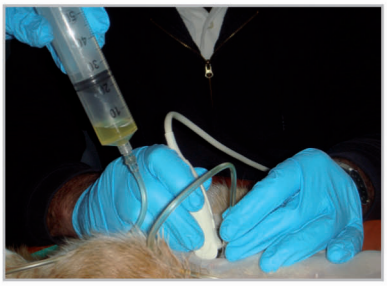
VETERINARY focus
Special edition
The worldwide journal for the companion animal veterinarian







Practical management of urinary tract disease

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ROYAL CANIN

Practical management of urinary tract disease

Table of contents

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Sarah Caney is a 1993 graduate of the University of Bristol (UK) where she also did her residency in Feline Medicine and PhD. She is an RCVS Specialist in Feline Medicine and enjoys seeing a mixture of first opinion and referral feline patients. She has written a number of books for cat owners and veterinary professionals including "Caring for a Cat With Lower Urinary Tract Disease" (co-authored with Danièlle Gunn-Moore) published by her company Cat Professional, a subdivision of Vet Professionals Ltd. (www.vetprofessionals.com). Sarah does a lot of owner-orientated feline research through online questionnaires and is especially interested in geriatric feline medicine.

Oscar Cortadellas

Oscar Cortadellas graduated from the Faculty of Veterinary Medicine, University of Zaragoza, Spain in 1989 and got his PhD from the University of Murcia in 2004. He has been working in private practice since 1990. His areas of special interest are nephrology, cardiology and infectious diseases. He has published several papers in national and international peer-reviewed journals. He has been a speaker in national and international congresses of Internal Medicine. Finally, he is the editor and co-author of a "Manual of Canine and Feline Clinical Nephrology and Urology".

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Marc Dhumeaux has worked extensively in small animal referral practices within France, Canada and the UK. He completed a Master of Veterinary Science in 2012 at the University of Saskatchewan. He is a Diplomate of the American and European Colleges of Veterinary Internal Medicine since 2012. His main areas of interest include urology and nephrology, immune mediated diseases and haematology. Marc Dhumeaux is one of the clinicians of the Internal Medicine service of the Pride Veterinary Centre, a large multidisciplinary referral hospital in the United Kingdom.

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Rafael Nickel graduated from Hanover Veterinary School in 1983 and made his Doctoral Thesis in 1986 on Laserspectroscopy. After an externship at TUFTS University in Boston, Massachusetts (1986-1987), he started working in private small animal practice in Germany. But from 1989 to 1997, he became assistant professor in Small Animal Surgery and then lecturer in Surgery and Urology at the University of Utrecht, Netherlands. Since 1993, he is a Diplomate of the European College of Veterinary Surgeons (ECVS), and he also made a PhD on urinary incontinence in 1998.

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Introduction

C. Renner

Advances are being made in the management of urinary conditions, but they often remain a source of difficulty for the general practitioner, discouragement for the owner and suffering for the animal.

Despite the progress achieved in nutrition, obstructed cats remain a medical emergency, and urinary catheterisation may prove to be a delicate procedure and can lead to sequelae. Urinary infections are too often recurrent, and cystocentesis, an essential procedure for a conclusive urinalysis, is not always straightforward in patients with lower urinary tract disease. In dogs, uroliths may recur even after surgical removal; while in cats, idiopathic cystitis needs to be fully explained to the owner in order to identify and reduce multiple aetiological factors. These are concrete examples of urinary difficulties.

In order to give you all the necessary elements to the practical management of the most common urinary conditions, we have asked a team of four European specialists to share their valuable experience in this Focus Special Edition. We can give them credit for having cleared up the confusion that surrounds these urinary conditions and for having identified the most frequent pitfalls that threaten the general practitioner. We hope that you will find this Focus Special Edition very enjoyable to read!

Philippe Marniquet,
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1. Treatment of urethral obstructions in male cats

> SUMMARY

The obstruction of the urethra in male cats is a frequent problem and is associated with significant morbidity and mortality. In emergency treatment, cystocentesis, analgesics and fluid therapy play an important role. Frequent complications are iatrogenic injury to the urethra by catheter placement, for which reason careful irrigation techniques should be used under optimal conditions. The prognosis and outcome depend on the cause; urethral plugs and spasm in idiopathic cystitis are frequent causes of relapse. The long-term prognosis following surgical treatment is generally considered to be good.

Introduction

Obstruction of the urethra in male cats is a frequently observed problem in small animal veterinary practice. The anatomy of the urethra in male cats, with a reduction in diameter of the penile part predisposes to this problem. The causes of obstruction (listed in order of decreasing frequency) are tissue and crystal formation (so-called urethral plugs), swelling and inflammation with spasms related to cystitis, as well as strictures; tumours are very rare (Saevik, 2011).

A study on the frequency of urethral obstruction in male cats in 24 American and Canadian university clinics during the period of 1980-1999 at first shows a proportionally averaged ratio of 19 cases out of 1,000 cats presented (Lekcharoensuk, 2002). However, over time, the relative frequency declined and in 1999 only 7 of 1,000 cats presented with this complaint. This was attributed to improved prevention of struvite crystal formation, which is the main component of urethral plugs.

Most small animal veterinarians have experience of managing urethral obstruction due to the frequency of this problem, regardless of their degree of specialisation. However, some treatment aspects still make this a relevant topic for discussion. A mortality of 8.5% is given for this in a relatively current study (Segev, 2011), and the number of urethral injuries due to catheter administration in blocked male cats is alarming. Catheter-induced trauma is the most frequent cause of urethral injuries in cats and the most frequent reason for surgical intervention (Corgozinho, 2007; Meige, 2008).

With consideration of current studies and findings, this article will describe, in a practical fashion, the most important aspects in the treatment of male cats with urethral obstruction. The approach to the male cat with suspicion of urethral obstruction is listed below step by step.

1/ The four steps

Step 1: Suspected diagnosis and assessment of patient

The animal owner's observation does not always allow a clear and definite statement on their animals' urination. Therefore, an anorectic, dehydrated male cat with considerably disturbed general condition may also suffer from the consequences of a urethral obstruction. In such cases, palpatory assessment of bladder filling, consistency of the bladder and pain sensitivity is also important. Unfortunately, there is no reliable scale that can substitute for the vet's experience. If urination occurs during the application of slowly increasing, careful pressure on the bladder area, then this can at least be used for ruling out urethral obstruction. A rather solid, slightly elastic consistency of a bladder which is around the size of a mandarin orange or larger would be cause for suspicion of urethral obstruction. Palpatory examination of the penis, as long as the patient allows this, can likewise give rise to causes for suspicion (*e.g.*, small stones and plugs can be felt). A definitive diagnosis, however, can only be made by obtaining radiographic images **(Figure 1)** as well as carefully placing a urethral catheter. Ultrasonographic images may also be quite helpful to provide evidence for obstruction or even to identify the cause **(Figure 2)**. Before this is carried out, we should take the following into account.

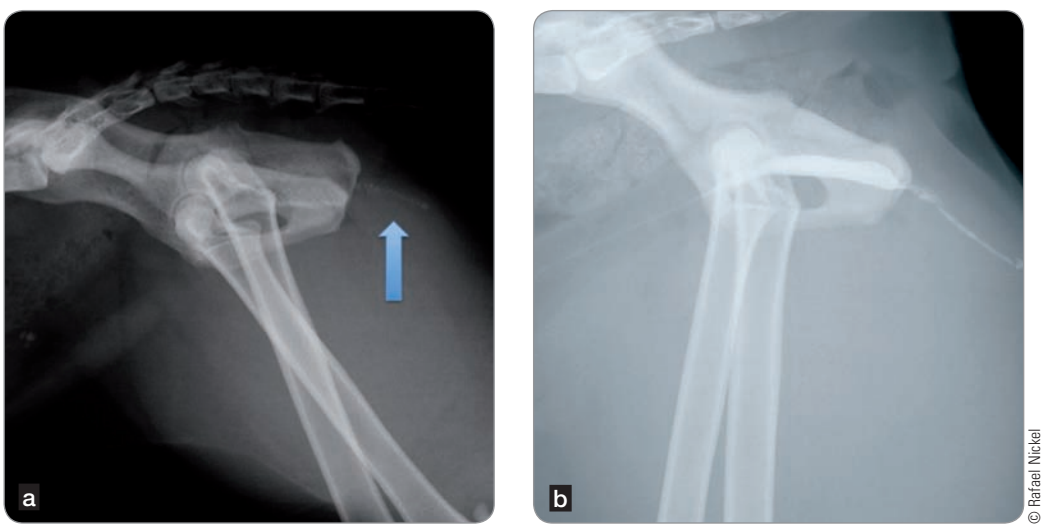
Step 2: Procedure for obstructed male cats in critical condition and/or severe pain

Cats can hold their urine for over 24 hours when the circumstances require it. We can therefore assume that periods of over 24 hours without urination are necessary in order to produce damage to the bladder wall, and more than 48 hours before the function of the kidneys is measurably disturbed (Bartges, 1996). For obstructed male cats with clearly reduced kidney function, hypothermia is frequently diagnosed (Fults and Herold, 2012).

The following aspects must be especially taken into account for management of emergency situations:

- An overfilled, stretched bladder is very painful for the animal.
- An overfilled, stretched bladder increasingly suffers a lack of oxygen.

Figure 1. Plain radiographic image of the urinary tract of a male cat with calcium oxalate urolithiasis in the bladder (a) and urethra (arrow). After flushing the urethra retrograde contrast radiography demonstrates mucosal lesions (b).



- Transport of urine from the kidneys to the bladder is no longer guaranteed.

Two initial measures in the event of emergency arise from this:
- administration of analgesics,
- decompression of the bladder.

Substances with no apparent negative influence on the cardiovascular system and which are not harmful to the kidneys in dehydrated patients are suitable as analgesics. Included under these is butorphanol at a dosage of 0.2-0.3 mg/kg bodyweight, which can be combined with midazolam at a dosage of 0.2 mg/kg bodyweight, and with this, a low-stress handling of the animal for further diagnostics is possible.

For the decompression of the bladder, its emptying through cystocentesis is recommended. The advantages (alleviation of pain, better oxygen supply, facilitation of urine passage from the kidneys to the bladder) clearly outweigh the disadvantages (perforation and leakage) and its application is simple and low-risk (Kruger, 1996). Though opinions on the methods vary, the author recommends that a 22G needle be used which is connected to an infusion extension, with this connected to a high-volume syringe **(Figure 3)**. Other clinicians may recommend a large-lumen needle (19-20G) open for puncture be used, with which excess pressure can be more quickly reduced and perforation and discharge of urine into the abdominal cavity prevented. However there are no scientific studies on this.

Based on experience, a complete emptying of the bladder, if possible, reduces the risk and extends the time until the next time bladder capacity is reached. The bladder capacity is quite variable and depends on the pathological changes of the bladder wall, however at least 5 mL/kg bodyweight may be expected. If we consider a post-obstructive increase in diuresis (Francis, 2010) and influence from fluid therapy, we must calculate at least 2 mL/kg bodyweight/hour of urine production, and with this, bladder capacity is possibly already reached by 3-4 hours after emptying.

In connection, or if necessary, simultaneously with the measures given above, further stabilisation measures should be carried out for critical patients depending on the results of the general clinic and a blood examination. Heat is foremost of these in the case of hypothermia, and fluid therapy in the case of dehydration, hypovolaemia and azotemia, hyperkalaemia and hyperphosphatemia. Confirmation of metabolic acidosis requires specific laboratory equipment, however acidosis is usually correlated with rising potassium levels in severe azotemia and is most often adequately addressed by fluid therapy.

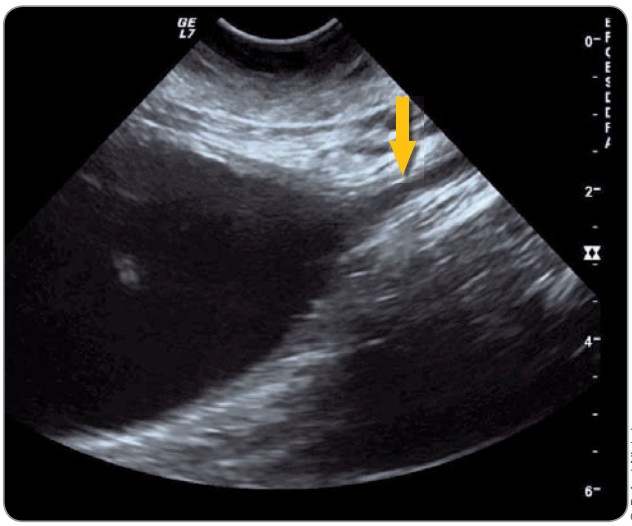


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Figure 2. Sonographic image of a distended bladder with urethral obstruction indicated by dilation of the proximal urethra (arrow).

For fluid therapy in the case of dehydration (generally, at least 5% are assumed to be in this situation), the infusion of an isotonic sodium chloride solution or a balanced electrolyte solution is suitable for the first 2-4 hours. The quantity is calculated according to the formula % dehydration x kg BW, so for a cat weighing 3 kg this would be approximately 150 mL (per 2-4 hours). On top of this is the maintenance requirement and compensation for fluid loss at 1-2 mL/kg/hour, respectively, which would be an additional 6-12 mL per hour for this example, so the cat would first have to have a minimum of approximately 50 mL/hour infused. For clear signs of hypovolaemia, bolus injections may also be applied over a few minutes, for which dosages of 10-30 mL/kg BW are recommended. For safe application of hypertonic or hyperosmolar solutions, further study of the literature on emergency medicine is recommended.

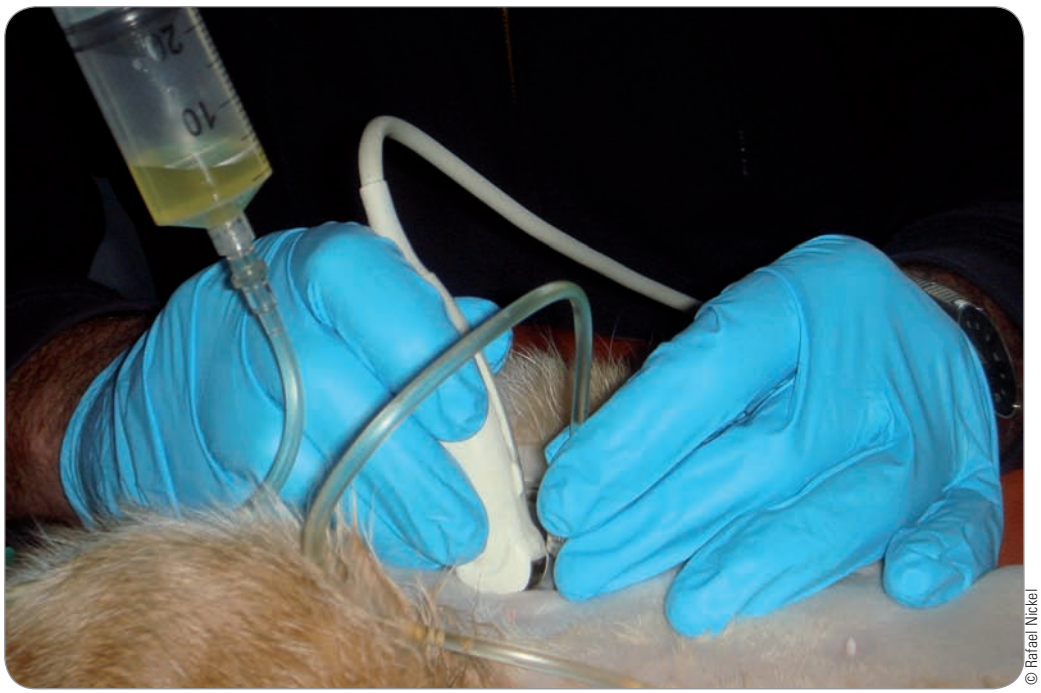


Figure 3. Demonstration of cystocentesis guided by sonography for management of acute obstruction. A large syringe allows faster emptying of the bladder, reducing the risk for rupture and leakage.

Step 3: Further diagnostics

Proof of the cause of an obstruction is only sensible after first implementing measures to stabilise the patient, if necessary and depending on the patient's condition. The urine collected during the cystocentesis can be examined, though this is difficult to interpret in the case of haemorrhagic changes in the bladder wall.

Important information for further procedures are:
- microscopic evidence of bacteria and leukocytes,
- crystals, and
- evidence or ruling out of glucosuria.

At this moment, other parameters cannot usually be reliably measured or assessed. A lack of evidence of crystals does not rule out the presence of bladder stones. In less critical conditions, the radiographic examination must be carried out earlier so the size and shape of the bladder can be estimated. After cystocentesis, the radiographic examination serves above all to find evidence of radio-opaque calculi. For this, it is very important to include the area of the penile urethra **(Figure 1)**. For the avoidance of stress and due to their ability to be interpreted, lateral projections suffice at first.

Should no indications as to the cause of the obstruction arise from either the clinical examination or the radiographs, then a urethral catheter may be carefully inserted in the urethra for purely diagnostic purposes. The smallest obstacle or crepitus should immediately be reason for terminating this procedure in order to cause no further irritation and to avoid iatrogenic trauma. In order to eliminate or flush out an obstacle, the conditions must first be optimised.

If there is no perceivable obstacle and the male cat is nevertheless unable to excrete urine, a retrograde contrast radiographic study **(Figures 1b and 4a)** should be considered in order to prove or rule out stenosis, strictures and other causes (Scrivani, 1997).

Step 4: Removing the obstruction

This last but most important step in the treatment requires optimal conditions in order to be successful and to avoid additional complications. Insertion of a catheter is the most frequent cause of urethral trauma in male cats (Corgozinho, 2007). The most frequently injured area is the dorsal portion of the junction between penile and pelvic urethra. This is due to previous damage caused by deposits or bladder stones and the natural angle of the penile urethra as it goes into the pelvic urethra **(Figures 4a and b)**.

For this reason, it is of the utmost importance to stretch the urethra and shift it into a level position. This is achieved by pulling the penis or prepuce in a caudal and dorsal direction. The catheter should have a diameter from 1 to 1.3 mm (3.5-5 French) and a sterile lubricating gel should be applied to the insertion end. During introduction of the catheter, as soon as crepitus or an obstacle are felt, we must immediately stop and move to irrigation **(Figure 5)**.

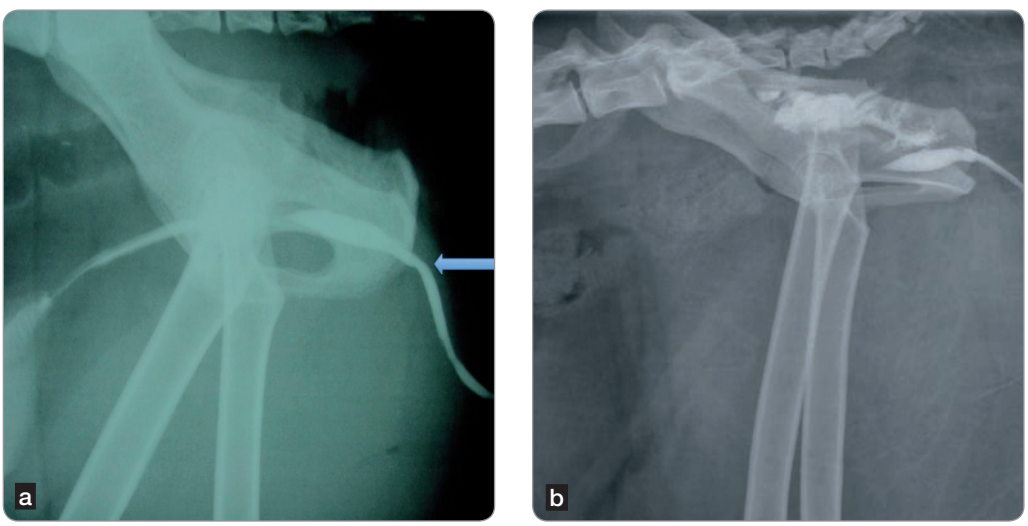
For the irrigation of the urethra, the following aspects are significant:

- Before this, the bladder should be emptied as much as possible by cystocentesis.
- The urethra should be relaxed.
- The cat should be sedated or under anaesthesia, so it has to be stabilised ahead of this.

Various approaches have been described for relaxing the urethra which can also increase the success rate of the irrigation attempt. For instance, the intra-urethral administration of atracurium besylate at 4 mL in a concentration of 0.5 mg/mL (Galluzzi, 2012). A coccygeal epidural anaesthesia can likewise be administered with a local anaesthetic, which in critical patients also allows the manipulation to be carried out under only light sedation (O'Hearn and Wright, 2011). Lidocain (2-4%) or mepivacain (1-2%) can be injected into the subdural space of cats in a total quantity of 0.8 to 1 mL at the lumbosacral joint or sacrococcygeal joint (Tacke and Bonath, 2014). Other local anaesthetics may also be used for this purpose.

In principle, the urethral musculature is mostly smooth musculature and innervated sympathetically and parasympathetically. The area of the outer sphincter is striated musculature and innervated somatically. With this, both medicines with anti-hypertensive potential as well as, for example, acepromazine, phenoxibenzamine

Figure 4. Retrograde contrast radiographic images of a male cat with an intact urethra (a) and another one with trauma induced by inappropriate catheter management (b). The arrow indicates the typical region for trauma caused by the catheter if the urethra is not pulled in a caudo-dorsal direction and straightened out.



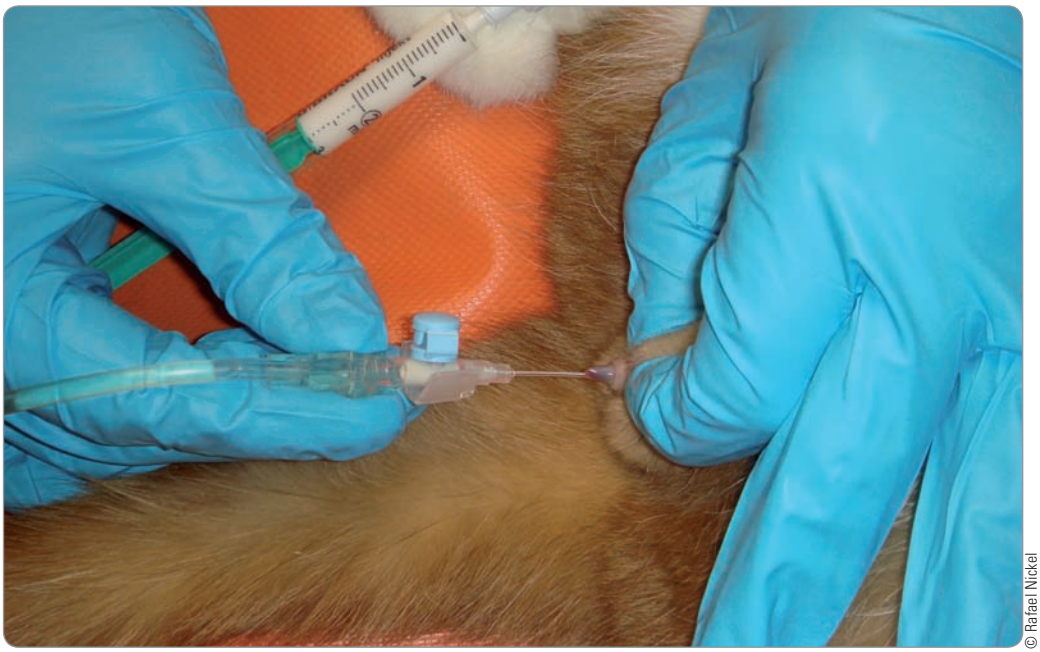


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Figure 5. Introduction of a catheter (a venous cannula here) for flushing of the urethra. One person pulls the prepuce in a caudo-dorsal direction and then advances the penis and introduces the catheter carefully with the other hand. A fluid extension set handled by another person makes the procedure much easier and allows less traumatic manipulation.

or prazosin are suitable to relax the urethra, but for the external sphincter, just a classic muscle relaxant such as diazepam or midazolam can be used.

When using acepromazine, we should take the long period of effectiveness into account and ensure that the patient has truly achieved sufficient cardiovascular and renal stabilisation. Then, in the case of an intramuscular dose of 0.25 mg/cat in combination with diazepam (0.2 mg/kg intravenously), a very effective relaxation of the urethra would be enabled. This way, plugs, deposits or solid calculi are more easily flushed from the urethra.

Optimal irrigation can be performed using a cannula, flexible venous catheter or urinary catheter with an atraumatic opening at the endpoint (20G, *e.g.*, 1-1.3 mm diameter, *e.g.,* 3.5-5 French) **(Figure 5)**. Classic urinary tract catheters have the opening on the side and therefore are not as suitable **(Figure 6)**. Optimal irrigation assumes that the urethra is widened and therefore all deposits can be more easily loosened. For this, the penis tip must be compressed over the cannula.

This is made easier using a moistened gauze. If there are enough assisting personnel, one person can hold the penis tip and introduce the cannula, which is connected through an extension (*e.g.*, infusion extension) to a syringe with isotonic sodium chloride solution, which another person operates. As soon as a jet is produced and the person holding the syringe cannot feel any resistance, the cannula can be pushed further in. If this is accomplished without resistance, another attempt can then be made to introduce a catheter.

2/ Catheter placement

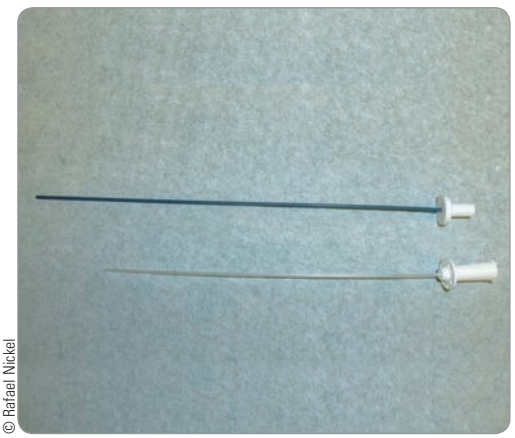
When a catheter is passed through the urethra without crepitus, it must be decided whether this should remain in the system. The decision criteria are as follows:

Indications for indwelling catheter with continuous urine collection:

- Azotemia or shift in electrolytes which require further intravenous fluid therapy.
- Bladder stones or significant amount of urine sediment which should be removed from the bladder surgically.
- Considerable reactions from the bladder wall (necrotic mucous membranes, blood-clots).
- The urethra has sustained considerable injuries (*e.g.*, trauma).

The catheter used as the indwelling catheter should be selected following consideration of their characteristics. Due to its elasticity, its Teflon coating and sufficient length, the author prefers the so-called "slippery sam" catheter (from SurgiVet, available in lengths of 11, 14 and 18 cm with diameter 3-3.5 French) **(Figure 6)**. This has a silicone disc at the end through which handles can be placed for fixation on the prepuce. Using various tube systems, the catheter can be connected to a collection system or urine collection bag; infusion extensions are likewise attached in a simple, effective and practical manner here. Empty infusion flasks with widened openings are also suitable as semi-closed systems for urine collection. The tube connections should be sufficiently long and not become tensed during movements by patients. A collar is necessary for protection of the catheter.

Figure 6. Different types of catheters for management of urethral obstruction in male cats. The upper type, a so-called slippery sam catheter, has teflon on its surface and is longer than the classic male cat catheter made from polyurethane. These are advantages in the long-term catheter management.



The time the catheter remains in place is handled differently in different clinics, and is obviously also judged according to individual criteria (kidney dysfunction, bladder condition, etc.). The preferred period is generally 3-5 days. In a retrospective study of 192 male cats with urethral obstructions, the period of catheter treatment was not statistically proven to be correlated with the relapse frequency, however the catheter's diameter was (Hetrick and Davidow, 2013). Relapse in cats for which a 3.5 French catheter was used was 19%, which was significantly higher than the group treated with a 5 French catheter (6.7%). In another study of 68 cats, however, the period of catheter treatment had a significant influence on the frequency of re-obstructions; the longer the catheter remained, the more seldom the relapse, with a total relapse rate of 15% (Eisenberg, 2013). In treatment of traumatic injury to the urethra, the catheter can be left under certain circumstances for up to 14 days (Meige, 2008).

In cases in which a catheter cannot be inserted in a retrograde fashion, this may be done via the antegrade route, for which a minimally invasive method is described. This can be performed under fluoroscopic guidance (Holmes, 2012). However, this method is often not effective in patients with calculi or strictures.

3/ Drug treatment

For cats in which no bladder stones are discernible in the system and no significant quantities of bladder sediment make a new obstruction likely, but merely soft plugs, spasms or cramping of the urethra are suspected as causes of the obstruction, catheter treatment can be forgone under certain circumstances. In one study on cost-effective management, 11 of 15 male cats could be successfully treated only through initial cystocentesis and administering of acepromazine, buprenorphine and medetomidine, as well as subcutaneous fluid application in appropriate cases, being released from the clinic within 72 hours. As a supplementary measure, the cats were placed in a quiet, dark, stress-free area (Cooper, 2010). However, 4 cats developed a uro- or haemoabdomen and 3 died.

In another study, 9 male cats with a diagnosis of an obstructive idiopathic cystitis had a glycosaminoglycan

product obtainable on the market instilled in the bladder. None of the male cats developed a new obstruction within an observation period of one week; 3 of 7 male cats relapsed in the control group (Bradley and Lappin, 2013).

In another study of 26 cats, lidocain and sodium bicarbonate were administered into the bladder by indwelling catheter once daily for 3 days, while the catheter was removed in the control group after 3 days. The relapse rate was almost the same, with 58% and 57% in both groups within 2 months (Zezza, 2012).

Medications that suppress tendencies toward spasms of the urethra are known as sympatholytics. We distinguish between drugs which selectively influence the musculature of the urogenital apparatus and less selective substances, such as butylscopolamine (known as buscopan in Germany and the UK) and acepromazine.

Though these substances are effective, the disadvantages due to the influence on intestinal activity or sedative secondary effects keep them from being the first choice in medical treatment. Prazosin was very successfully used for a long time, which led even less to relapse of obstructions in male cats as compared with use of phenoxybenzamine (Hetrick and Davidow, 2013). Unfortunately, this is no longer available in many countries. However, due to their pharmacological properties, similar substances could be considered such as terazosin, doxazosin, tamsolusin or alfuzosin, and could be redesignated for use in veterinary medicine.

In cats, the impeding effect of the above-given selective alpha-blockers on the hypogastric nerve, and so the sympathetic innervation of the urethra, is proven (Ramage and Wyllie, 1995; Lefevre-Borg, 1993), but dose-effect curves and controlled studies providing evidence of the effects in symptomatic patients only exist in human medicine. Tolerance and compatibility study data is also available for cats from registration trials, such as for example alfuzosin (xatral, Sanofi Aventis Product Monograph). A dosage range can be derived from this, in which, at present, dosages around 1 mg/kg BW are assumed to be safe and effective for cats. In practice, a 2.5 mg tablet was repeatedly used by the author with no perceivable problems.

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Figure 7. Urethral spasm can be a cause of significant pain and difficulty urinating.

Pain during urination can lead to urethral spasms **(Figure 7)**, which correspond to a somatic detrusor-urethral dyssynergia. Here, the relaxation of the diagonal external sphincter has also been empirically proven with a muscle relaxant. Diazepam is then applied orally, rectally or i.m. and, if necessary, i.v. at a dose of 0.25 mg/kg BW.

4/ Surgical treatment

If we consider the prognosis of urethral obstructions in male cats, then a total relapse rate of 15% and 24% or 43% arises respectively after medical and catheter treatment (Hetrick and Davidow, 2013; Eisenberg, 2013; Gerber, 2008). After the cause was differentiated, a relapse of urethral plugs was most frequent (Gerber, 2008).

Surgical treatment is not normally the first choice for management of urethral obstruction. Straightforward indications for surgical treatment include:

- injury/trauma of the penile urethra,
- stricture/stenosis of the penile urethra,
- bladder stones that cannot be moved through irrigation,
- cellulitis affecting the perineal area,
- neoplasia affecting the penile urethra.

The procedure may also be considered depending on:
- severity and number of relapses,
- cost-benefit analysis for repeated conservative treatment,
- long-term prognosis.

In a Norwegian study of 86 cats, the follow-up after perineal urethrostomy was examined over an observation period of up to 10 years. The perioperative mortality was 6%, relapse rate of severe urinary tract symptoms was 11% and the animal owner's satisfaction was 88% (Ruda and Heiene, 2012). If we consider these figures against the results of a study from Switzerland in which 21% of male cats were euthanised at the animal owner's wish due to relapsing obstruction (Gerber, 2008), then perhaps the decision for surgical intervention should not be made too late.

Since the penile urethra in male cats has a considerably smaller diameter than the pelvic urethra (ca. 1-1.3 mm *vs.* ca. 3-5 mm), the general principle of urethrostomy is not only to guarantee undisturbed passage of urine through a connection of the pelvic urethra to the skin, but also of that of tissue plugs and stones in the event of relapse. There are several varied approaches and methods for urethrostomy in cats, for which the reader is referred to the specialist surgical literature. The generally most common methods and those preferred by the author are described on pages 16 and 17.

Description of perineal urethrostomy

The patient may be positioned in ventral recumbency, rear legs hanging over the table, the tail drawn forward. Some also prefer the patient laying in dorsal recumbency with rear legs brought forward. A purse-string suture with synthetic, non-absorbable monofilament suture material of 3-0 thickness on the anus can optionally be applied. After shaving, the perineum is prepared for surgery. An ellipsoid incision is made around the prepuce, the dorsal aspect of this being as wide as possible and extending to just under the anus.

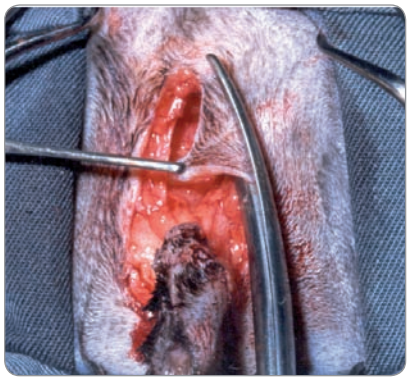


Figure 1. The prepuce has already been dissected and the skin is now removed with Metzenbaum scissors. This should achieve a wound size for creation of an appropriate stoma.

The skin and prepuce are carefully removed from the penis **(Figure 1)**. Then the subcutaneous tissue of the perineum is carefully dissected with spreading movements of the dissecting scissors from the penis and underlying musculature. The ischiocavernosus muscle on both sides becomes visible **(Figure 2a)**. It is prepared so that it can be completely visualized and then cut through with scissors **(Figure 2b)**. Total dissection must be achieved. Then you can pull the penis further back, until the bulbourethral glands lying paired together are visible dorsolaterally. The urethra must only be dissected bluntly at the ventral aspect from the pelvic floor. The retractor penis muscle, located dorsally is then removed **(Figure 3)**.

The corpus spongiosum urethrae becomes visible underneath. The penis tip is then cut off 3-5 mm higher with scissors. The bleeding corpus cavernosum is grabbed from below with an arterial clamp, so that the bleeding stops and the rest of the penis can be moved back.

With small scissors or a scalpel, the urethra can then be split at the dorsal aspect up to the bulbourethral glands **(Figure 4)**. The wide part of the urethra begins here **(Figure 5a)**. Check that there is sufficient opening using a urinary tract catheter with French gauge 6-8 (2-2.6 mm). It should pass easily **(Figure 5b)**.

Then you can begin suturing. Four individual anchors are necessary to hold the urethra open, so that you are able to see the inside of it, with the split part running distally spread as far apart as possible. The first anchors are placed only between the subcutaneous tissue and the tunica albuginea of the corpus cavernosum **(Figure 6)**.

Figure 2. Illustration of the stage when the prepuce and the tip of the penis have already been dissected.
(a) A very important structure to identify and dissect is the bilateral ischiocavernosus muscle.
(b) Only after complete dissection of this muscle can the wide pelvic part of the urethra be advanced sufficiently.

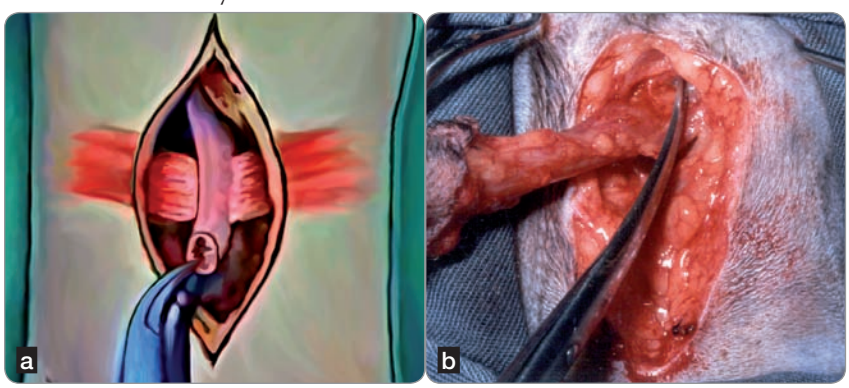
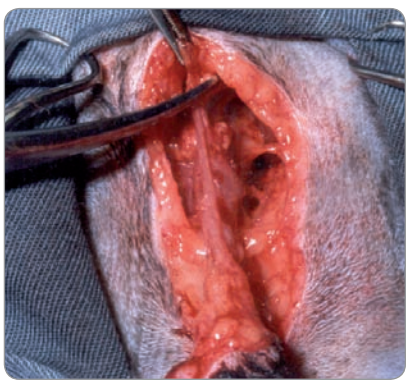


Figure 3. Dissection of the retractor penis muscle allows visualization of the corpus cavernosum urethrae, recognized by a pale blue appearance.



in male cats (Nickel, 1992; Nickel and Peppler, 2014)

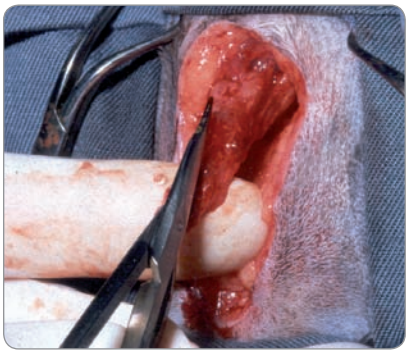


Figure 4. Iris scissors are used to incise the dorsal aspect of the urethra up to the level of the bulbourethral glands.

The suture material for these anchors and the following ones is either absorbable, multifilament, synthetic material (4-0 or 5-0 USP; *e.g.*, Polyglactin) or monofilament material according to personal preference. After the anchoring, the skin is sutured to the mucosa. Simple or continuous sutures are possible **(Figure 7)**. Sutures are recommended all around the urethra opening. It is best to stick the needle from the mucosa out toward the skin, and the knots should lie on the skin. For safety reasons, a collar should be applied for quite a long period (at least 10 days). Further measures are aimed at addressing the cause of the obstruction and its complications (see also the other examples in this issue).

Long-term complications of a perineal urethrostomy are attributed either to poor tissue perfusion, weak local host defence mechanisms, failure of the surgical technique or self-mutilation (Nickel, 1995). The most common factor leading to stricture formation is inappropriate dissection of skin and ischiocavernosus muscle (Nickel, 1995). Relatively high bacterial urinary tract infection rates of up to 16% were reported in the long-term post-operative period (Nickel 1995). However, this figure is similar to that reported in a recent retrospective study of causes of FLUTD in Norwegian cats without urethrostomy (15%, Saevik 2011).

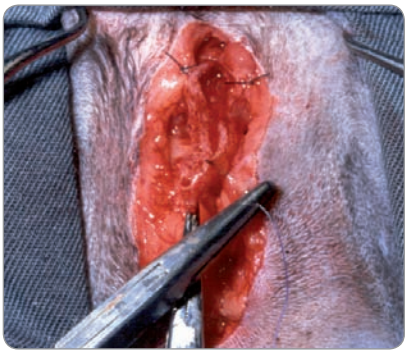


Figure 6. Sutures placed in the subdermal layer and the corpus spongiosum of the penis using suture material size 4-0 USP.

Figure 5. Illustration of the penile urethra dissected up to the level of the bulbourethral glands. This is where the urethral diameter of the pelvic urethra is sufficient to create the stoma (a). Then it is possible to insert a catheter with a diameter of 2-2.6 mm (6-8 French) (b).

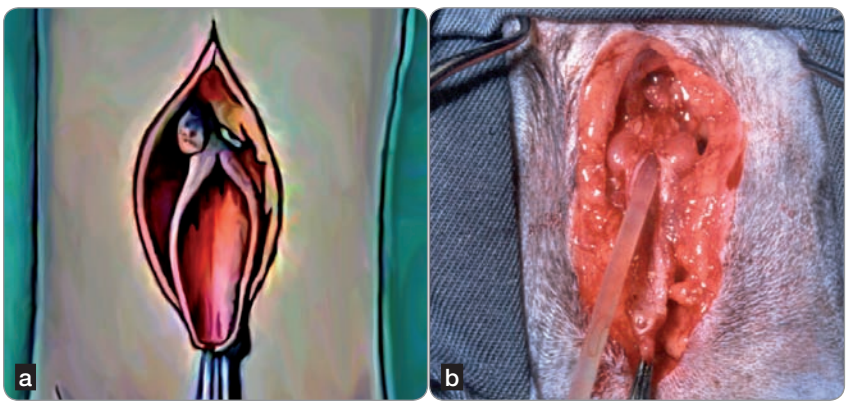
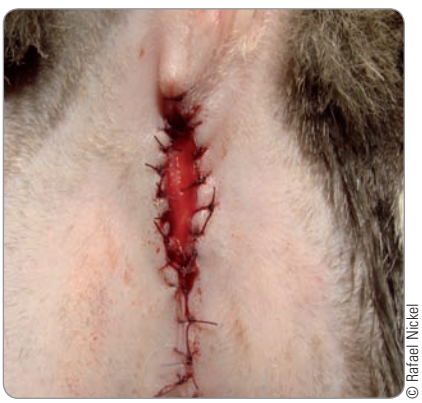


Figure 7. Sutures between skin and urethral mucosa have been placed and the penile urethra is pulled laterally to provide a barrier against healing of the dermal wound edges to each other. This would lead to stricture formation and recurrence of obstruction.



2. Feline idiopathic cystitis

> SUMMARY

Feline lower urinary tract disease (FLUTD) is an important cause of illness, affecting an estimated 7% of cats (Bartges, 2002). Feline idiopathic cystitis (FIC) is diagnosed in more than half of cats with FLUTD under the age of ten years. FIC is a diagnosis of exclusion – in other words, known causes of FLUTD such as urolithiasis and bacterial urinary tract infections must be ruled out before making this diagnosis.

There is no single effective treatment for FIC. Instead, successful management depends upon a long-term commitment and team approach between carer, veterinarian and cat. Research studies have shown that it is possible to greatly reduce the frequency and severity of episodes of FIC for the vast majority of affected cats through identifying and addressing potential sources of stress to the affected cat and pursuing tactics that help the cat to produce more dilute urine. In some patients, additional treatments such as spasmolytics can be helpful.

1/ Introduction

Feline lower urinary tract disease (FLUTD) is a term used to encompass a number of conditions which affect the bladder and urethra and which may be associated with inappropriate urination. FLUTD is most common in young and middle aged cats. There are several important medical causes of FLUTD but idiopathic FLUTD – also known as feline idiopathic cystitis (FIC) – is the most common by far.

FIC is especially common in young and middle aged cats where it accounts for more than 50% of cases of FLUTD (Bartges, 2002). Other risk factors include being overweight or obese and having a sedentary lifestyle (Buffington, 2006). FIC can be obstructive or non-obstructive and can present in four different ways:

- single acute, self-limiting episode of clinical signs (most common),
- frequent recurrent episodes of clinical signs,
- persistent clinical signs,
- urethral obstruction (male cats) – this requires emergency treatment.

Clinical signs with non-obstructive FIC are most commonly self-limiting – in other words, the cats get better on their own, usually within five to ten days. However, many affected cats suffer from repeated episodes of clinical signs which can be very distressing to both cat and owner. In general the frequency and severity of these episodes gradually decreases with time.

Unfortunately, in spite of more than thirty years of research, no one knows the precise cause of FIC. Complex interactions between the cat's environment, nervous system, stress-response and bladder are involved. Stress is now known to play a very important role in triggering and/or exacerbating FIC and cats suffering from FIC may in fact be suffering from what has recently been described as "Pandora syndrome" (Buffington, 2006;

Buffington, 2011; Stella, 2011). Cats suffering from "Pandora syndrome" have clinical signs affecting other organ systems such as the gastrointestinal tract, skin, respiratory tract, central nervous system, cardiovascular or immune systems in addition to their lower urinary tract signs. These "sickness behaviours" include non-specific clinical signs such as vomiting, diarrhoea, decreased food and water intake, fever, lethargy, enhanced pain-like behaviour, changed grooming behaviour and decreased social interactions (Stella, 2011). For cats suffering from "Pandora syndrome", FIC may be the bladder's manifestation of a systemic disorder (Buffington 2011). Unpredictable, inescapable periods of stress are most likely to be associated with clinical signs of any or all of these organ systems. The most common sickness behaviours reported in association with changes to the normal routine are vomiting, diarrhoea, inappropriate urination, inappropriate defecation and inappetence (Stella, 2011). "Pandora syndrome" may result from early adverse experiences that sensitise the neuraxis to sensory input. This results in an increased activation of the stress-response system when this susceptible individual is placed in a provocative (stressful) environment (Buffington, 2011).

Clinical signs of FIC may wax and wane in association with stress and usually respond to environmental modifications aimed at resolving the cause of the stress. The causes of chronic stress suggested to be most damaging are those over which the cat has little or no control.

2/ Diagnosis of FIC

FIC is a diagnosis of exclusion. Important differential diagnoses include urolithiasis, bacterial urinary tract infection, bladder tumours and incontinence. In cases presenting for the first time with clinical signs of FLUTD it may not be appropriate to perform all diagnostics but persistent and repeat episodes should be investigated thoroughly where possible. Diagnosis of FIC depends on a thorough approach with particular attention paid to clinical signs affecting other organs ("Pandora syndrome") and a behavioural history.

a. Take a thorough medical history

This is a vital initial step in the assessment of patients and involves questioning to determine the nature and severity of the lower urinary tract signs. Important questions include:

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Figure 1. Dysuria and periuria are common features of FIC.

- Is this the cat's first episode or have there been lower urinary tract problems in the past?
- What is the cat's current dietary regime? Wet or dry catfood? Standard catfood or specially formulated prescription diet?
- How long has this (and any prior episode) lasted?
- Is the cat able to pass urine or is urethral obstruction suspected?
- What clinical signs are currently present? Dysuria, pollakiuria, stranguria, haematuria, periuria (urination in inappropriate locations) and passing small quantities of urine are the most common signs of FLUTD **(Figure 1)**.

Questioning should also establish whether other clinical signs consistent with "Pandora syndrome" are present.

b. Take a thorough behavioural history

This is especially important in persistent and recurrent cases of FIC where identifying and addressing sources of stress are vital to successful management of this condition. Questioning should establish:

- The number of cats in the household and whether the cats have access outside.
- The number, location, substrate and hygiene procedure for any litter boxes in the home.
- The number of social groups in the household. Conflict between cats is an especially common cause of stress. In order to address this, care needs to be taken

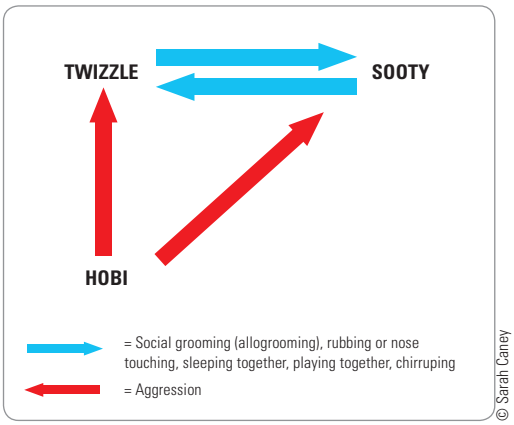

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Figure 2. Identifying the number of social groups within the household is essential in understanding what resources to provide for the cats. The diagram shows social interaction between three cats living in one household. Sooty and Twizzle are in the same social group, both enjoying grooming and interacting together. Hobi only shows aggressive behaviour towards Sooty and Twizzle and is therefore in a different social group.

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Figure 3. Stress associated with overcrowding and conflict with other cats is a common risk factor for FIC.

to understand the number of social groups within the home and determine whether there are adequate resources for each social group. Each social group needs access to litter boxes or other toileting facilities, food, water, somewhere to rest/hide and safe entry and exit routes. Some cats, especially the elderly, have specific requirements for feline or human companionship. Several social groups may exist in the home and each of these needs its own separate resources.

To assess how many social groups there are in a household, close observation of the cats' behaviour is necessary. Cats in the same social group show affiliative behaviour such as mutual grooming, touching noses and chirruping whilst cats in separate social groups do not. It can be helpful to ask the carer to write the names of all of their cats on a piece of paper and then draw arrows between the names whenever they see the cat show affiliative behaviour to another cat. This helps to build up a picture of the social groups in the home **(Figure 2)**. Some cats can be in more than one group so it can get a little complicated.

- Is there any conflict between the FIC cat and other cats known of? Signs of conflict can be subtle and do not always include active signs of aggression. Signs of passive aggression include staring or blocking access to a litter box or catflap.

- Do cats outside the household have any direct or indirect contact with the FIC cat? Indirect contact would include observing the FIC cat when it is using a litter tray which some cats find intimidating.

- Are there any other known stressors or trigger factors which may have been responsible for the FIC episode, such as:
  - overpopulated household or neighbourhood **(Figure 3)**,
  - new pet recently introduced to the household or neighbourhood,
  - return of a cat into the household after a period of absence,
  - excessive and intrusive physical contact and interaction from the owner,
  - overprotective and/or stressed owner,
  - frequent changes to the normal routine such as trips away, visitors,
  - new baby **(Figure 4)**.

It can be helpful to draw a map of the home environment marking out resources, escape routes and locations of periuria.

c. Perform a physical examination to help rule out other causes of FLUTD

For example, identifying weight loss in a patient suffering

Figure 4. Changes to the household such as a new baby or new dog can be a source of stress to cats.

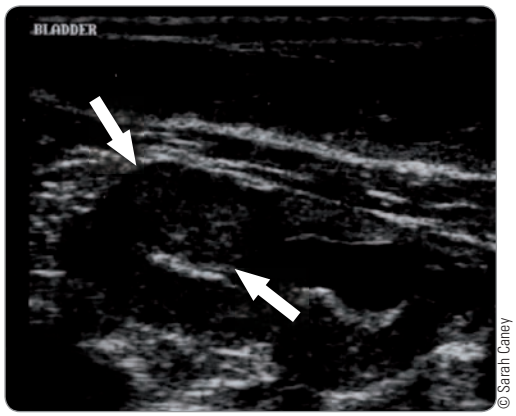


Figure 5. Ultrasound of the bladder of a cat with a bladder tumour – the bladder wall (indicated with arrows) is thickened and irregular.

from neoplasia or a paralysed tail in a cat with a spinal injury.

d. Perform a urinalysis

The aim of urinalysis is to rule out other causes of FLUTD such as bacterial urinary tract infections. In general, cystocentesis is the preferred method for urine collection, but this can be challenging in cats with FIC since they will tend to empty their bladder frequently. Ultrasound guidance can assist sampling in cats with small bladders. Typically cats with FIC will have very concentrated urine (USG > 1.050) with haematuria a common feature.

e. Haematology and serum biochemistry profiles

These are very important in cats suffering from urethral obstruction to assess for serious abnormalities that might occur such as dehydration, hypocalcaemia and hyperkalaemia. Blood profiles are also potentially helpful in chronic/persistent/recurrent cases of FLUTD where it is important to look for underlying or concurrent systemic disease which may affect management. Common examples in an older cat would include renal disease and hyperthyroidism where bacterial urinary tract infections are an acknowledged complication.

f. Diagnostic imaging (radiography, ultrasonography)

It is helpful to look for stones in the bladder and/or urethra, tumours and other problems **(Figure 5)**. Cats suffering from an episode of FIC tend to have empty bladder on ultrasound; the bladder wall may appear thickened and sediment/deposit may be visible internally.

3/ Treatment of FIC

Optimal treatment of FIC depends on making an accurate diagnosis. Although non-obstructive FIC is considered to be a self-limiting, problem treatment is usually recommended since this is such a painful and debilitating condition. Unfortunately, very few treatments have been assessed in a rigorous way. Since FIC usually resolves spontaneously, many treatments can appear to be effective when in fact the cat is making a spontaneous recovery. All of the current medical treatments for FIC are palliative – aiming to support the cat through an episode and reduce the risk of further episodes from occurring. The biggest long-term improvements are seen using a dual approach to reduce stress and encourage the cat to produce dilute urine.

A) Strategies to reduce stress in the home

Efforts should be focussed on identifying and addressing potential causes of stress in the home as discussed earlier. In severe cases, referral to a veterinary behavioural expert may be valuable to accurately diagnose and resolve causes of chronic stress.

Synthetic F3 feline pheromones preparations such as Feliway (Ceva Animal Health) can be helpful in reducing tension found in multi-cat households. These act as a confirmatory signal that the environment is safe and therefore must be used in conjunction with other environmental management, such as ensuring that there are adequate litter boxes and so on. Feliway alone is not sufficient to prevent signs of FIC associated with stress but it can be very helpful if introduced just prior to periods of increased stress – for example if a new baby is to be introduced to the house (Gunn-Moore and Cameron, 2004).

Environmental enrichment is also beneficial as a means of reducing stress. Examples of positive ways of improving a cat's environment include provision of climbing frames with resting areas and playing games that stimulate natural cat behaviour **(Figure 6)**.

Restricting (or reducing) the number of cats in the home to socially compatible levels and resisting the temptation to expand the household by introducing new cats will help to reduce the incidence of stress-related diseases like FIC. In some situations, rehoming the FIC cat to a household where it will be the only cat is an effective strategy.

B) Litter box management

Cats suffering from FIC should be provided with a litter box. The ideal litter box is safe, secure and private with no conflict associated with using this area of the home (or outside if this is where the cat urinates). In multi-cat households there should be sufficient litter boxes to cater to all of the social groups and these should be positioned in such a way that the cat does not have to pass cats from other social groups to access the litter box. The number of litter boxes should correlate with the number of social groups in the household. Covered litter boxes can be unpopular with some cats as they can leave them vulnerable to an ambush by another cat. Litter box hygiene is essential so that there is nothing to put a cat off toileting in the box.

Twice daily (or more often) scooping of urine and faeces is essential, and full cleaning of the box with replacement of the litter should take place at least once a week. The litter type should be selected to be one which the cat likes to use – perfumed or uncomfortable litters (*e.g.*, some cats dislike different consistencies of litter) should be avoided. The depth of the litter has been shown to be important in encouraging appropriate toileting behaviour – where possible deep litter boxes should be used and filled so that the cat can dig and bury its urine and faeces deposits adequately. Most cats prefer to use a fine, sandy clumping litter with a 3 cm depth in the litter box. In older cats, deep litter boxes can be difficult to climb into so a ramp might be needed. Alternatively, a tray with a shallow entrance (like a potting tray) can be used, or you can cut a shallow-sided entrance into a normal litter box.

What is MEMO and is this helpful when managing cats with FIC?

MEMO or multimodal environmental modification is an acronym coined by Professor Tony Buffington and his colleagues at Ohio State University, where much research on FIC has been conducted. MEMO encompasses many of the treatments already discussed (behavioural modifications, tactics to encourage fluid intake) through use of owner questionnaires and interviews followed by individualised treatment recommendations. In one of their publications Professor Buffington and his colleagues demonstrated that MEMO was effective in resolving around 70-75% of cats with severe FIC and greatly reduced the severity of signs and frequency of relapses in the remaining cats (Buffington, 2006).

For those cats suffering from periuria, soiled areas should be cleaned thoroughly to reduce the risk of future soiling in this area. The site affected should first be cleaned using a 10% solution of biological or enzymatic washing powder. Once cleaned, the area should be rinsed with water and allowed to dry. Once fully dry, the area should be sprayed with surgical alcohol using a plant mister and left to dry again. Deodorising preparations are available to help remove the smell of cat urine and some of these can be very effective.

All of these measures are designed to break down and remove all scent marking proteins, pheromones and other substances which might encourage a cat to use this area again as a latrine. Badly affected portions of carpet may need to be removed and replaced in some cases. If possible the cat should be kept away from the site – for example by moving furniture to cover a portion of affected carpet or blocking access.

Figure 6. Climbing frames can offer environmental enrichment. Picture included with kind permission of Professor Danièlle Gunn-Moore.

C) Strategies to encourage production of less concentrated urine

The cat will be less likely to suffer from episodes of FIC if they produce more dilute urine (Markwell, 1999). The aim is for the cat to be producing urine with a specific gravity around 1.035. This encourages frequent urination and dilutes any irritant components of the urine. Producing dilute urine does not treat the underlying cause of FIC, so issues such as stress also need to be addressed.

Where possible a moist food should be offered – cats will typically produce 50% more urine if their diet is switched from dry to wet, indicating that they naturally do not choose to drink much when fed standard dry cat food. Methods to encourage drinking include:

- Choosing a bowl which the cat likes to use – generally this means glass, metal or ceramic rather than plastic bowls. Cats usually prefer wide, shallow bowls which are filled to the brim, but it is worth experimenting to find the best solution for each individual cat **(Figure 7)**.
- Offer several bowls of water around the house and avoid putting the water bowl next to the food bowl. Cats have evolved to choose water sources away from food sources since these may be contaminated.
- Some cats like running water – drinking fountains, running taps, showers etc.
- Offering tasty liquids such as the juice from a defrosted pack of prawns (or by liquidising some prawns in water) can be popular.
- Feeding moist rather than dry food to encourage fluid intake. Some cats with a preference for dry foods will tolerate water being added to this – even if the end result looks somewhat unappealing!
- Feeding a diet specially formulated to encourage drinking by stimulating the cat's sense of thirst, such as Royal Canin Urinary S/O. These diets are especially helpful for those FIC cats that will only eat dry food.

D) Weight management in obese cats with FIC

Obesity management is indicated in overweight/obese cats suffering from FIC.

Figure 7. It is worth experimenting with different types of water bowls to see whether the cat has a preference for one type over another (a-c). Some cats like to drink from fountains and other running water sources (d).

E) Other medical treatments for FIC

A number of medical treatments may be suggested in cats with FIC. These include:

- Analgesics and anti-inflammatories: while analgesics (*e.g.*, Buprenorphine 10-30 mcg/kg PO, SC or IM TID-QID) have not been shown to alter the course of FIC, they can help an affected cat to feel more comfortable. Glucocorticoid steroid drugs such as prednisolone have been shown to be ineffective in treating FIC (Osborne, 1996).
- Therapy for urethral spasm may be helpful in some cases. Smooth muscle anti-spasmodics include acepromazine (0.05-0.2 mg/kg IV, IM or SC; 1-3 mg/kg PO); prazosin (0.25-1.0 mg per cat PO BID-TID); phenoxybenzamine (0.5-1.0 mg/kg PO BID) and amitriptyline (0.5-1.0 mg/kg PO SID). Skeletal muscle anti-spasmodics include dantrolene (0.5-2.0 mg/kg PO BID).
- Glycosaminoglycan (GAG) supplements: GAG supplements are believed to work by attaching to the lining of the bladder and reducing the permeability of this to noxious substances. Unfortunately, several clinical studies have shown that GAG supplements are not

generally effective in the majority of cats affected by FIC (Gunn-Moore and Shenoy, 2004; Chew, 2009).

- Tricyclic antidepressants (TCAs): this group of drugs have been found to be helpful in some people with interstitial cystitis and hence have also been trialled in cats with FIC. TCAs have a number of effects including increased bladder capacity, urethral and ureteric relaxation, anti-inflammatory, analgesic and antidepressant effects. Although anecdotal reports exist supporting use of Amitriptyline in cats (0.5-1.0 mg/kg orally every evening weaning down to the lowest effective dose), the two published placebo-controlled studies did not report any benefits (Kraijer, 2003, Kruger, 2003). Both of these studies were short-term and it may be that a longer treatment period is needed to show a benefit. TCAs are probably best reserved for cats with chronic intractable disease or when a known stressful event can be predicted, such as a house move. Clomipramine (0.25-0.5 mg/kg PO every evening weaning down to the lowest effective dose) has been more commonly used for urine spraying (King, 2004; Landsberg and Wilson, 2005). Side effects of TCAs include urine retention, constipation, sleepiness and raised liver enzymes.

- Alpha-casozepine: this nutritional supplement is made from a protein present in cow's milk and has been reported to have positive effects on treating anxiety in cats (Beata, 2007). It may be helpful for short-term stresses (such as moving house) as well as more long-term stress management. There are many anecdotal reports of benefits in cats with FIC although published data is still lacking.

4/ Summary

FIC is an important cause of morbidity in cats and can be a distressing condition for both cat and carer. The best success rates are achieved by using a multimodal approach taking consideration of all of the factors discussed in this article. Owner commitment is key since success primarily depends on actions on their part.

3. Update on the diagnosis and treatment of urinary tract infections

> SUMMARY

Urinary tract infections (UTIs) are a common finding in canine and feline practice, and their management is not always easy; relapses and reinfections occur relatively often. The clinician needs to keep in mind that not all patients with a UTI have clinical signs of urinary tract disease, and not all patients with clinical signs of urinary tract disease have a UTI. Thus, it is important to make a complete diagnostic evaluation in each particular case. Regarding the treatment, the selection of the antibiotic should be based on the results of the antibiotic susceptibility test, and its duration will depend on whether the infection is a simple or a complicated one.

Introduction

Urinary tract infection (UTI) is defined as the adherence, proliferation and persistence of an infectious agent (generally bacteria, but occasionally also fungi, viruses, mycoplasmas or parasites) in areas of the urinary tract that are normally sterile.

Between 5-27% of all dogs suffer from a UTI at some point in their life (Smee, 2013). The prevalence is highest in spayed females, followed by neutered males and non-spayed females (Cohn, 2003). Such infections are more frequent in elderly animals (over 7-8 years of age), but can also be found in young individuals, generally due to the existence of congenital anatomical anomalies of the urinary tract that predispose to UTIs (Kivistö, 1977).

In cats, the prevalence of UTIs varies between 2% (Kruger, 1991) and 43% (Lees, 1996), with great variability depending on the age of the animals. A study found that only 2% of 143 cats under 10 years of age with lower urinary tract disease suffered from UTIs, while this percentage increased to 45% in cats over 10 years of age (Bartges, 2000).

1/ Aetiopathogenesis

Under normal conditions, the vagina, vestibule, prepuce and distal urethra have an important resident microflora, while the rest of the urinary tract territories are sterile. Most UTIs are a consequence of the ascending migration of bacteria from the distal portions of the urogenital tract or from the gastrointestinal tract, crossing the perineal barrier, colonizing the external genitalia and reaching the urethra and bladder. UTIs resulting from haematogenous spread are infrequent. Because of the close relationship between the different components of the urinary tract, involvement of one area increases the probability of involvement of other locations.

Table 1. Defence mechanisms of the urinary tract against urinary tract infections (Modified from Senior, 2011).

Resident flora	The resident flora occupies urinary epithelial receptors and consumes micronutrients, thereby complicating the consolidation of other pathogenic bacteria.
Urine composition	Urea in urine has antibacterial properties. The high urine osmolality inhibits bacterial growth (very important in cats). Very acid pH values have antibacterial effects. Ammonia has antibacterial effects.
Urethra	The urethral epithelium can trap bacteria, thereby preventing them from accessing proximal regions of the urinary tract. The existence of high pressure zones in the middle urethra avoids bacterial ascent.
Prostate	Antibacterial activity of the prostatic secretions.
Urinary bladder	Forceful and complete bladder voiding clears bacteria that may have ascended through the urethra. The glycosaminoglycans of the bladder urothelium inhibit bacterial adherence.
Ureter	Distal urine flow (from kidney to bladder) complicates bacterial ascent. The oblique intramural course of the ureters in the bladder facilitates their closure when the bladder is filled.
Kidneys	Glomerular mesangial cells High renal blood flow

However, the urinary tract possesses natural resistance against infection **(Table 1)**, which under normal conditions prevents such microorganisms from producing a UTI. These defence mechanisms must suffer alterations in order for a UTI to develop **(Table 2)**.

Over 75% of all UTIs (up to 90% according to some studies) in the dog and cat are caused by a single pathogen (Barsanti, 2012). In this context, *E. coli* is the most common causal agent in both animal species **(Figure 1)**. Recent studies have reported an increase in the prevalence of infections caused by *Staphylococcus felis* in the cat (Litster, 2007-2009). While infrequent, UTIs produced by *Corynebacterium urealyticum* represent a challenge for clinicians, due to its slow growth *in vitro*, the seriousness of the clinical condition and the multiresistant nature of the organism against many antibiotics. Although there have been reports of UTIs caused by *Mycoplasma spp.*, their role as urological pathogens has not been fully established (Barsanti, 2012).

Multiple infections are more common in complicated cases characterized by the existence of an underlying anomaly (anatomical or functional alterations of the urinary tract). In such cases it is important to confirm that the isolated bacteria are the cause of the infection, not simply contaminants.

The presence of fungi and yeasts in a urine sample may be the result of contamination or defective processing. However, their presence in samples that have been correctly obtained and processed is considered abnormal and may require treatment.

2/ Clinical manifestations

The clinical manifestations of UTIs are highly variable and depend on the virulence of the infecting agent, the host immune system and the duration and location of the infection. The most characteristic manifestations include haematuria, dysuria, periuria (urination in inappropriate places), pollakiuria, stranguria (straining to urinate) and pain in response to bladder palpation. However, in many patients with systemic disease (*e.g.*, diabetes mellitus, hyperadrenocorticism, hyperthyroidism), the infections are asymptomatic, and the existing manifestations are those of the underlying

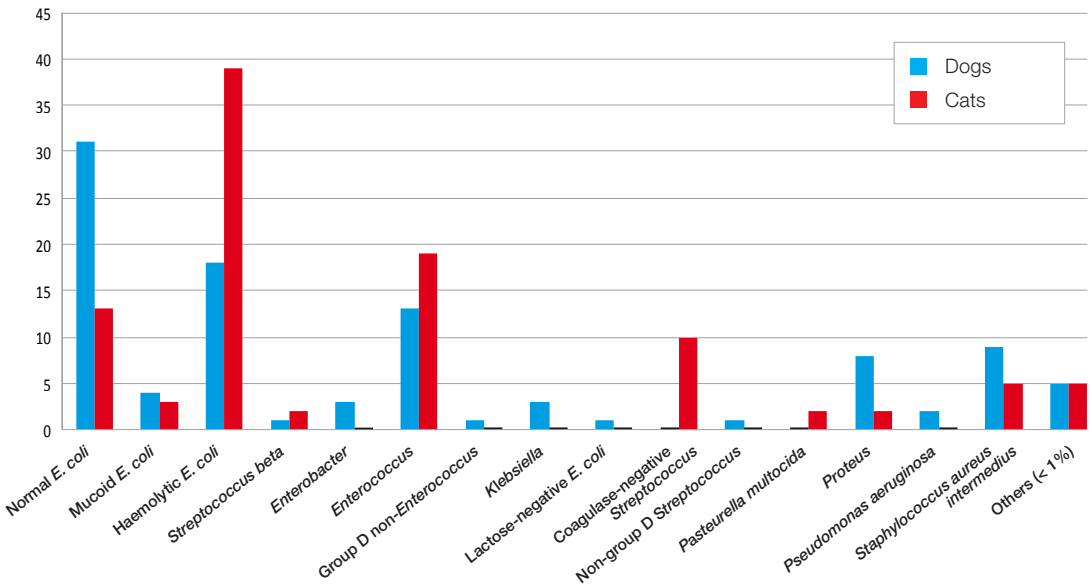


Figure 1. Bacteria associated with urinary tract infections in dogs and cats. Samples obtained by cystocentesis. OSU Microbiology Laboratory, January 2000-April 2007. The organisms listed as < 1% (< 5% of the total) include *Acinetobacter, Citrobacter, Clostridium,* coagulase-negative *Staphylococcus, Corynebacterium spp., Klebsiella oxytoca, Lactobacillus, Malassezia, Mycoplasma, Pasteurella multocida, Pasteurella spp., Pseudomonas spp., Serratia* and yeasts in dogs; and *Corynebacterium, Enterobacter, Klebsiella,* lactose-negative *E. coli, Pasteurella spp., Morganella, Serratia* and yeasts in cats (Chew, 2011).

disorder (Forrester, 1999; Bailiff, 2006). Animals with acute pyelonephritis may show signs of sepsis and pain in response to renal palpation, while polyuria/polydipsia may be the only clinical manifestation in animals with chronic pyelonephritis. In patients with subclinical bacteruria, we should consider the possible existence of underlying disease (endocrine, metabolic) or a urinary tract anomaly favouring the presence of bacteria in regions of the urinary tract that are normally sterile.

3/ Diagnosis

The minimum diagnostic evaluation in any patient with a suspected UTI must include the compilation of a case history, physical examination, and urine tests (urine specific gravity, urine dipstick and microscopic examination of the sediment). In addition, urine culture is indicated, followed by antibiotic susceptibility testing (Weese, 2011). These tests are indicated not only when there is a clinical suspicion of a UTI, but also when a condition associated with an alteration of defensive mechanisms of the urinary tract is present **(Table 2)**.

In order to correctly interpret the urine tests, the samples must be obtained by cystocentesis. Many patients with dysuria/pollakiuria present with a small or empty bladder when seen in the clinic – a situation that complicates the procedure. In these cases the administration of an analgesic injection followed by resting in the cage helps fill the bladder and obtain the required urine sample.

To avoid false negative or positive bacteriological results, samples that cannot be processed immediately must be refrigerated and sent to the laboratory within 24 hours, (Weese, 2011). If this is not possible, the use of preservatives can be discussed with the laboratory, but boric acid should not be used as it can inhibit bacterial growth (Rowlands, 2011).

The urine of these patients is generally hypersthenuric, except in the case of animals with underlying disease (*e.g.*, chronic kidney disease, hyperadrenocorticism), in which the urine may be isosthenuric or even hyposthenuric.

Dipstick testing usually reveals haematuria, proteinuria and an increase in leukocyte count (note: dipsticks are unreliable for assessing leukocytes). Proteinuria is usually postrenal. If proteinuric kidney disease is suspected, it is advisable to repeat the evaluation once treatment for the UTI has been completed.

The presence of pyuria (defined as over 3 leukocytes per x 40 magnification field) indicates inflammation but not necessarily a UTI. In contrast, the identification of bacteria in urine samples obtained by cystocentesis followed by adequate processing is indicative of a UTI. Sediment from animals with pyelonephritis may contain granular cylinders or racket-shaped cells originating from the renal pelvis, though these are not constant findings. On the other hand, in dilute urine or when the bacterial burden of the sample is low, bacterial detection in the sediment may prove difficult. In order to increase the sensitivity of the detection of bacteruria, it is advisable to examine the sediment in stained samples, *e.g.*, using the modified Wright stain (Swenson, 2011) or Gram staining (Way, 2013).

In animals with a deficient immune response (hyperadrenocorticism, feline leukaemia), a UTI may be present without associated inflammation. Systematic urine culture in patients with isosthenuric/hyposthenuric urine is only justified if the sediment findings are suggestive of a possible UTI (Tivapasi, 2009).

A recent study has found a rapid enzyme test (Accutest Uriscreen™) to be more sensitive but less specific than urine sediment examination in diagnosing UTIs. Accordingly, a negative enzyme test helps to rule out the possibility of a UTI, although a positive result requires culture confirmation (Kvitko-White, 2013).

Quantitative urine culture is the gold standard for diagnosing UTIs. Practically any growth in a sample obtained by cystocentesis is significant, though most patients with a UTI yield over 10^3 cfu/mL. In samples obtained by catheterization, counts of over 10^4 cfu/mL (males) or 10^5 cfu/mL (females) are required. Samples obtained by spontaneous micturition can show growths of over 10^5 cfu/mL as a result of contamination by resident flora. Such samples therefore should not be used for urine culture (Weese, 2011). In the case of a positive culture, antibiotic susceptibility testing should be obtained. Many veterinary laboratories report the results of the bacterial susceptibility tests for each antibiotic tested as susceptible (S), intermediate susceptible (I) and resistant (R). An "S" indicates that the infection may be appropriately treated with the recommended dosage of antimicrobial agent. An "I" suggests that the response rates may be lower than those for susceptible isolates, but that the antimicrobial can still be effective if it can achieve high concentrations in urine. An "R" indicates that the antibiotic is unlikely to be effective. In many cases this information assists decision-making regarding the management of a UTI. However, it must be taken into account that many laboratories perform their test using agar disk diffusion (*i.e.*, Kirby-Bauer technique) which is based on the serum (not the urine) antibiotic concentration. Thus, an antibiotic that reaches high concentrations in urine may still be

Table 2. Causes of altered defence mechanisms against urinary tract infections.

- Altered bladder voiding
- Endocrine diseases
  - Hyperadrenocorticism
  - Diabetes mellitus
  - Hyperthyroidism
- Chronic prostatitis
- Urethral catheterization
- Anatomical alterations
  - Ectopic ureter
  - Infantile or recessed vulva
  - Vestibulo-vaginal stenosis
- Chronic kidney disease
- Immunosuppressants
  - Corticosteroids
  - Azathioprine
  - Cyclosporine
- Chemotherapeutic agents
- Urolithiasis
- Urinary tract neoplasms
- Urinary tract surgery
- Urethral obstruction
- Urinary incontinence
- Disc disease

Table 3. Dosage and mean urine concentration of some antibiotics.

Antibiotic	Dose (mg/kg)	Administration route	Mean urine concentration ± SD µg/mL
Amikacin	5 tid 10 bid 15 sid	SC SC/IM	342 ± 143
Amoxicillin	12 tid	PO	202 ± 93
Ampicillin	26 tid	PO	309 ± 55
Cephalexin	35 bid	PO	500
Cefovecin	8 mg	SC	2.9 (14 days after, dog) 0.7 (14 days after, cat)
Chloramphenicol	35 tid	PO	124 ± 40
Doxycycline	5 bid	PO	53 ± 24
Enrofloxacin	2.5-5 bid	PO	40 ± 10
Gentamycin	6 sid	SC	107 ± 33
Kanamycin	5 tid	SC	530 ± 151
Nitrofurantoin	4.4 tid	PO	100
Tetracycline	20 tid	PO	138 ± 65
Tobramycin	2.2 tid	SC	145 ± 86
Trimethoprim-sulfadiazine	15 tid	PO	55 ± 19 (based on trimethoprim fraction)

effective in spite of being considered as "I" or even "R" in the susceptibility test. To evaluate this possibility it is important to ask the laboratory about the minimum inhibitory concentration (MIC) of the evaluated antibiotics and to know their mean urine concentration (MUC). The MIC is the minimum concentration of an antimicrobial drug that will inhibit the growth of the uropathogen.

It is accepted that if the MUC **(Table 3)** is at least 4 times the MIC, the antibiotic will be effective (Senior, 2011). For example if the laboratory reports that for a particular uropathogen the enrofloxacin MIC is 4 µg/mL this antibiotic will probably be effective, because its MUC is 40 ± 10 µg/mL. However, if for the same bacterial isolation, the trimethoprim/sulfadiazine MIC is 20 µg/mL this drug won't be effective. Although this approach is valid in many UTIs, the clinician should consider that in cases where there is some underlying renal or prostatic condition, or if a deep adherence of the bacteria to the urothelium is suspected, it is better to select the antibiotic according to its plasma concentration.

In addition to the above tests, in patients with complicated infections we may need to use other laboratory procedures (haematology, biochemistry, serology) and/or imaging techniques (X-rays, ultrasound, endoscopy) to facilitate the diagnosis of associated disorders **(Figure 2)**.

4/ Treatment

A) Treatment of simple infections

Simple infections are sporadic infections in the bladder of an animal without other disorders and with an

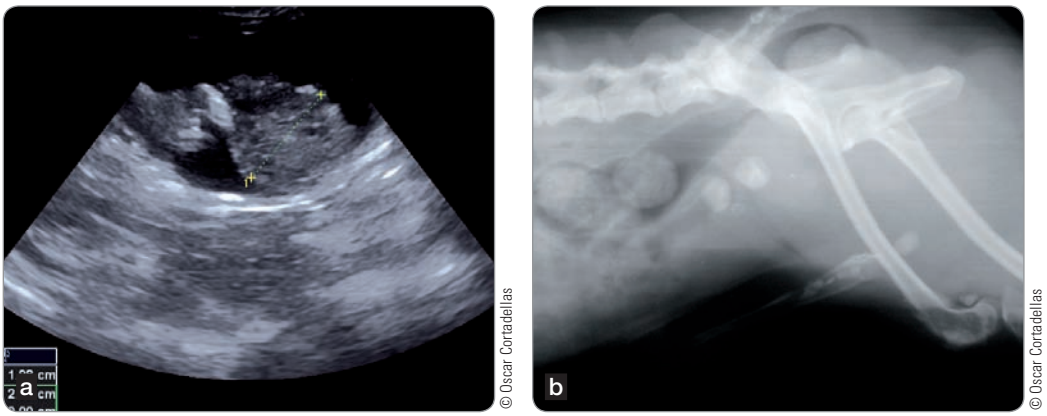


Figure 2. (a) Abdominal ultrasound. Longitudinal section of the bladder. Intravesical mass in a cat with haematuria unsuccessfully treated with antibiotics (without previous urine culture) for four weeks. (b) Abdominal X-ray of a Yorkshire Terrier with haematuria and intermittent dysuria for 7 months, treated with antibiotics and analgesics on several occasions, with partial remission of the clinical signs. Presence of radio-opaque uroliths in the bladder and penile urethra.

anatomically and functionally normal urinary tract (Weese, 2011).

In human clinical practice these infections are treated with antibiotics for 1-5 days. In veterinary practice there is scant evidence regarding the optimum duration of treatment, though antibiotics are generally provided for 10-14 days. In any case, most animals show remission of the signs within 48-72 hours. A recent study in dogs with simple UTIs concluded that enrofloxacin at a dose of 18-20 mg/kg/24 hours for 3 days offers efficacy similar to that of amoxicillin/clavulanate 13.75-25 mg/kg/12 hours for 14 days (Westropp, 2012). However, it must be noted that the administration of such doses of enrofloxacin in cats is not advised, and that the efficacy of other antibiotics in short courses has not yet been established. In any case, the International Society for Companion Animal Infectious Diseases (ISCAID) recommends the treatment of uncomplicated UTIs for 7 days (Weese, 2011).

The choice of antibiotic should be based on the findings of the antibiotic susceptibility testing. However, if we wish to start treatment before these results become available, or if antibiotic susceptibility testing is not possible, then empirical therapy can be provided. In this context the ISCAID recommends amoxicillin (11-15 mg/kg/8 hours) or trimethoprim/sulfonamide (15 mg/kg/12 hours). Although the combination of amoxicillin/clavulanate (12.5-25 mg/kg/8 hours) may be equally effective, there is no evidence of additional benefits compared with the other proposed treatment options (Weese, 2011).

Alternatively, the choice of antibiotic can be made on the basis of the results of the urine tests. Most *cocci* (*Staphylococcus spp.*, *Enterococcus spp.* and *Streptococcus spp.*) and bacilli in alkaline urine (*Proteus spp.*) are sensitive to ampicillin, amoxicillin/clavulanate, cephalosporins and potentiated sulfonamides. *S. intermedius* and *Proteus mirabilis* produce beta-lactamases; as a result, in these cases, amoxicillin/clavulanate may be preferable. In dogs, many UTIs caused by these bacteria are associated with struvite uroliths. Consequently, whenever these pathogens are isolated, it is advisable to evaluate patients for the possible presence of stones. The presence of bacilli in acid urine generally corresponds to *E. coli* or, less often, to *Klebsiella spp.*, *Pseudomonas spp.* or *Enterobacter spp.*, while observed *cocci* generally correspond to *Enterococcus spp.* or *Streptococcus spp.* The sensitivity of bacilli in acid or neutral urine is less predictive, and in these cases an antibiotic susceptibility testing is therefore required. When *P. aeruginosa* is suspected, the fluoroquinolones are generally a good first choice (Senior, 2011).

While waiting for the culture results, another option is to provide treatment according to the Gram staining results - administering amoxicillin/clavulanate in the

case of Gram-positive organisms and fluoroquinolone in the presence of Gram-negative organisms.

The traditional recommendation is to perform urine culture 5-7 days after the end of treatment to confirm its efficacy. However, in the absence of clinical signs, there is no evidence supporting the need for such cultures (Weese, 2011).

B) Treatment of complicated infections

Complicated UTIs are defined as ≥ 3 UTIs per year (recurrent UTI), or UTIs detected in animals with anatomical or functional alterations of the urinary tract, or with underlying disease conditions predisposing to infection, its persistence or recurrence, or treatment failure (Weese, 2011).

Treatment is provided for 4-6 weeks and should be based on the results of the antibiotic susceptibility testing. When this is not possible, use can be made of the antibiotics indicated in cases of uncomplicated UTI (preferably drugs not previously used in the patient in question) (Weese, 2011).

Shorter treatments probably can be used in animals with non-recurrent complicated infections. In order to improve collaboration on the part of some owners (*i.e.*, treatment compliance), it may be preferable to use antibiotics requiring few doses a day, or long-acting antibiotic injections. The bacteria colonize the prostate gland in a full 90% of all non-castrated males. Consequently, in these cases it is advisable to choose an antibiotic according to its capacity to penetrate the prostate gland (*e.g.*, fluoroquinolones, trimethoprim/sulfonamide, doxycycline, carbenicillin and chloramphenicol) (Senior, 2011). In multiple infections, we should choose an antibiotic that is effective against all of the isolated bacteria. If this is not possible, then treatment should be targeted to the most relevant pathogen. Some authors consider that in the presence of *Enterococcus spp.*, the infection can be resolved by treating the associated pathogen.

It is advisable to repeat urine culture 5-7 days after starting treatment (the result being negative if the antibiotic is effective) and again 7 days after the end of therapy (3 weeks in the case of treatment with cefovecin).

If pyelonephritis is suspected, treatment should be started without first waiting for the culture results. Antibiotics with activity against Gram-negative species are recommended, in view of their high prevalence in pyelonephritis (Weese, 2011).

Treatment is not advised in patients with subclinical bacteruria, unless the urine sediment findings indicate active infection or there is a risk of ascendant or systemic infectious spread (*e.g.*, animals with kidney disease, immunosuppression, hyperthyroidism or a risk of struvite lithiasis). Although there is no evidence in veterinary practice, in humans it has been shown that antibiotic treatment of women with asymptomatic bacteruria offers no benefit and even favours the future development of symptomatic UTI.

Urethral catheterization is one of the situations that predispose to UTIs, particularly when the catheter is kept in place for prolonged periods of time. Indiscriminate urethral catheter use should therefore be avoided, and when needed, catheterization should be as brief as possible (Bubenik, 2007). Prophylactic antibiotics and the treatment of catheterized animals in which asymptomatic bacteruria has been detected should be avoided, since both circumstances favour the development of antibiotic resistance. Treatment with antibiotics should be reserved for those patients with clinical manifestations of a UTI. In these cases urine culture is always required. If possible, treatment should start once the catheter has been removed. Alternatively, the catheter should be replaced, and a urine sample should be obtained for culture. The duration of treatment depends on whether the infection is simple or complicated. Culture of the catheter tip or of samples obtained through the catheter or from the reservoir bag is not advised (Weese, 2011). Patients at risk may benefit from urine culture once the catheter has been removed, although in the absence of clinical signs or in low risk situations, there is no evidence supporting the need for culture.

C) Treatment failure

Treatment of UTIs should result in disappearance of the clinical signs and receipt of a negative urine culture result. If this is not achieved, then the possible causes must be investigated. The first step is to check that the

prescribed antibiotic dosage and regimen have been correct, that the owner has administered the treatment as indicated, and that the drug has been absorbed. If all the above is found to be correct, the next step is to perform a urine culture; the results obtained will guide the subsequent decision-making process **(Figure 3)**. If the additional diagnostic evaluation or the therapeutic management required in these patients can not be performed properly, it is advisable to refer them to a specialist.

5/ Relapse and reinfection

Relapse is defined by the development of a UTI in the first 6 months after the end of treatment that was considered to be successful, with isolation of the same pathogen as in the initial infectious episode. Reinfection in turn refers to a UTI in which the isolated pathogen is different from that identified in the initial episode. Relapse often occurs before reinfection, though this is not always the case. It must be taken into account that apparent relapse may actually represent reinfection produced by different strains of the same species. In such situations the only way to distinguish between relapse and reinfection is to perform a bacterial genotypic study.

Relapse means that the infection was not completely eradicated. This is often attributable to the use of an inadequate antibiotic dose. Alternatively, the drug may fail to reach adequate concentrations at the site of infection, for instance in situations where the pathogen is "walled off" by inflammatory tissue. This is common in chronic prostatitis in non-castrated males, and in pyelonephritis, or in cases of struvite urolithiasis. Relapses should be regarded as complicated infections, and should be treated as such. However, it is sometimes difficult to reach the bacterial nidus or location, and the prognosis can be affected as a result.

Reinfection is related to the existence of predisposing causes that have not been eliminated. In these cases treatment should be based on the findings of the antibiotic susceptibility testing, and the underlying causal factors should be addressed as far as possible. If thorough diagnostic evaluation is unable to identify the predisposing causes, or if these cannot be eliminated, then preventive treatment can be provided, once the initial episode of UTI has been cleared.

6/ Prevention

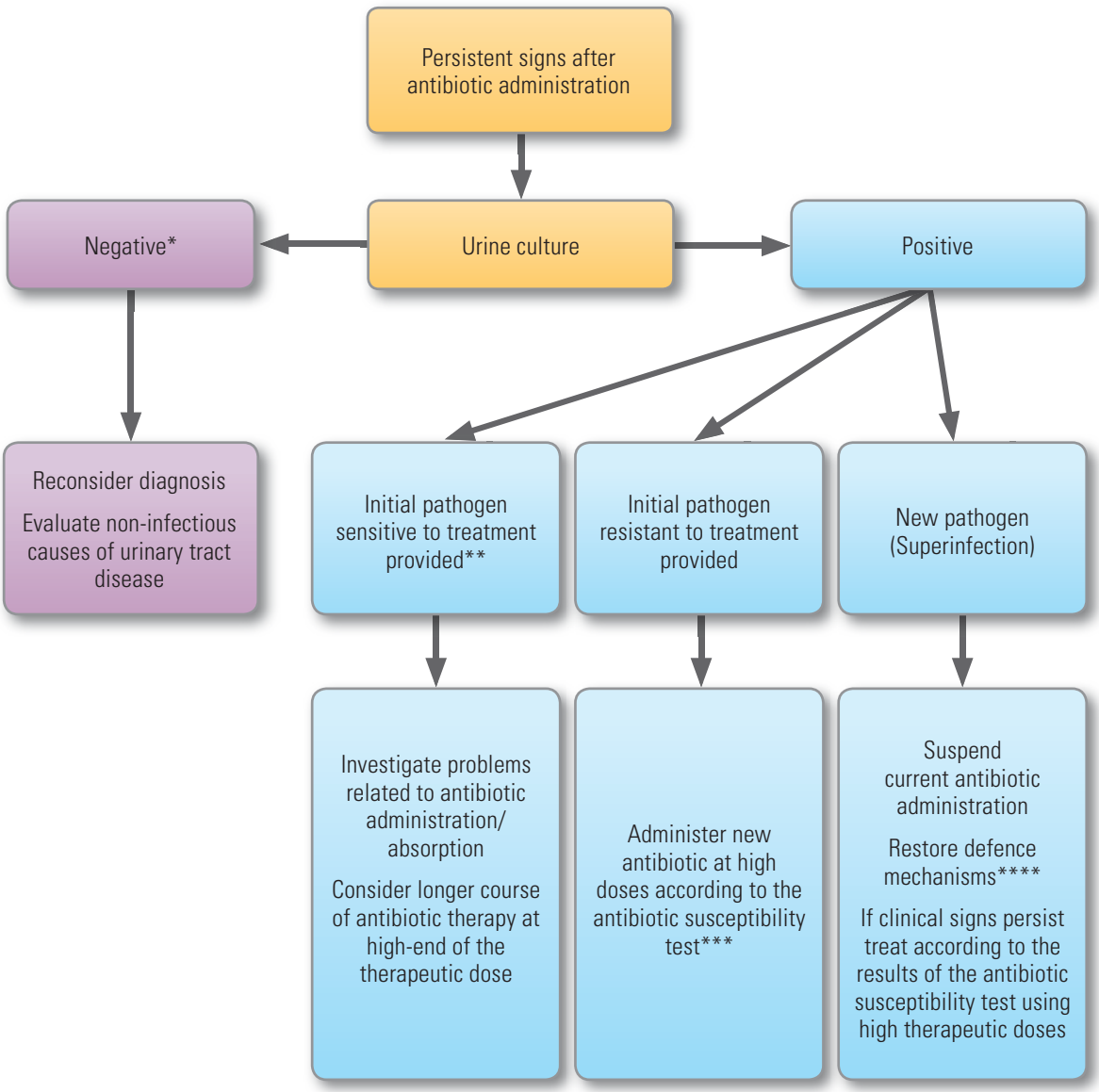
One preventive option, after eliminating the initial infection (that is, after a negative culture has been obtained) is to administer low dose antibiotics that are eliminated in the urine (30-50% of the usual therapeutic dose), for prolonged periods of time (6 months or more). The antibiotic should be administered at night in order to ensure longer persistence in the urine. Urine cultures should be performed on a monthly basis in order to prevent the development of bacterial resistance. If bacterial growth is observed, the UTI should be treated according to the findings of the antibiotic susceptibility testing. If the cultures remain negative after 6-9 months of treatment, we can suspend therapy and monitor for possible recurrences (Lulich, 2004; Senior, 2011). Although this strategy may be effective in some patients, the supporting evidence is limited. On the other hand, the possible development of bacterial resistance must be strongly considered before starting this kind of therapy.

Other preventive strategies include the administration of methenamine, cranberry juice extract, mannose or probiotics. In any case, the evidence on which these treatments are based is still limited. Further studies are therefore needed before they can be recommended on a routine basis.

Methenamine is a urinary antiseptic with possible beneficial effects attributable to the fact that an acid pH converts it into formaldehyde, which has anti-bacterial actions. Methenamine is probably less effective in infections with urease-producing pathogens that increase urine pH. The addition of an acidifying agent would therefore be advisable in such cases. Methenamine is not advised in pregnant or nursing patients or in individuals with liver or kidney failure. Side effects are more frequent in cats than in dogs, and include mainly nausea, anorexia, vomiting and methaemoglobinaemia (Bowles, 2012).

In human medical practice, the consumption of cranberry extracts has been shown to reduce UTI recurrences by 35-40% (Masson, 2009). Although similar evidence is

Figure 3. Flowchart of the possible causes of a lack of treatment response in urinary tract infections.



* In animals with a history of uroliths, consider the possibility of a false negative result. Different studies have shown between 18.5% (Hamaide, 1998) and 23.8% (Gatoria, 2006) of all cultures in dogs with a UTI and urolithiasis to be negative in urine and positive when culturing the urinary stone or bladder mucosa.

** In relapsing UTIs caused by *E. coli*, there is evidence that the antibiotic susceptibility testing findings do not allow us to definitively determine whether the infecting strain is the same (Freigtag, 2006).

*** In these cases some authors suggest suspending the treatment with the purpose of modifying the bacterial resistance patterns. Although this strategy has been shown to be effective in some cases, it is essential to consider the potential risks of leaving the infected animal without treatment (Lulich, 2004).

**** Superinfections are normally due to the coexistence of a process favouring infection (*e.g.*, prolonged urethral catheterization, antepubic urethrostomies).

lacking in veterinary practice, a recent study has concluded that cranberry extracts reduce the uro-epithelial adhesion capacity of *E. coli* by 30% (Smee, 2011). There is no evidence regarding efficacy in infections caused by other pathogens. Cranberry extracts possibly increase the urinary excretion of oxalate. Therefore, until this aspect has been clarified, it is not advisable to administer such extracts to patients with a history of urolithiasis (Bowles, 2012).

Some experimental studies have postulated that mannose could reduce the adhesion of certain strains of *E. coli* to the urinary epithelium. This effect has not been evaluated in cats and dogs, however (Kukanich, 2013). On the other hand, the use of probiotics could contribute to minimising relapses through modifying the bacterial flora, displacing urological pathogens and creating an environment unfavourable to the growth of certain microorganisms. At present, there is no evidence to recommend their use in dogs and cats with UTIs.

7/ Treatment of fungal urinary tract infection

Urinary tract infections caused by fungi are uncommon, representing less than 1% of all UTIs in dogs and cats, and are associated with immunosuppression or local immunodeficiencies that cannot be fully corrected (Pressler, 2011). The main causal agent is *Candida albicans*, though other *Candida* species and different fungi can also be isolated (*Aspergillus spp.*, *Blastomyces spp.*, *Cryptococcus spp.*). The tentative diagnosis can be established on identifying fungal elements in the urine sediment, though it is important to perform a urine culture to correctly identify the infecting species. *Candida spp.* tend to grow on blood agar plates in the first 48 hours, though in the event of prior suspicion of funguria, the laboratory can be instructed to perform culture in Sabouraud agar.

In asymptomatic patients, treatment of the underlying cause often eliminates fungal growth. If there are clinical signs, or when the underlying cause cannot be corrected, specific treatment must be provided. Of the different antifungals used in veterinary practice, only fluconazole and amphotericin B are actively excreted in the urine. Taking into account the ease of administration and the possible side effects, we should initially use fluconazole for 4-6 weeks, with repeat urine cultures performed every 2-3 weeks (Pressler, 2011). In cases of resistance, we can administer clotrimazole or amphotericin B via the intravesical route.

4. Management of uroliths in dogs and cats

> SUMMARY

Uroliths are a common cause of urinary tract disease in dogs and cats. This chapter reviews the mechanisms of formation of the three most common types of uroliths in both species: struvite, calcium oxalate and ammonium urate. Treatment options for dissolution and ablation of uroliths are explained and recommendations to prevent recurrence in predisposed patients are given.

Introduction

Urinary stones, or uroliths, are a frequent cause of urinary tract disease in dogs and cats. Clinical signs frequently associated with stones include haematuria, abdominal pain and recurring urinary tract infections. Stones lodged in the urethra may be responsible for complete urinary obstruction, which can have severe consequences if the obstruction is not addressed in a timely fashion. The stones formed in the renal pelvis may cause pyelic or ureteral obstruction. Unilateral obstructions of the upper urinary tract are not always immediately associated with clinical signs in the animal, but they can nevertheless lead to irreversible renal lesions.

In this chapter, we will focus on the three most common types of stones in dogs and cats: struvite, calcium oxalate and ammonium urate. Detailed knowledge of the factors predisposing to stone formation, as well as their physical and chemical characteristics, allow the clinician to design the best therapeutic plan for their elimination and the prevention of recurrence.

1/ Mechanism of formation of urinary stones

Urine is naturally an aqueous environment intended to dispose of metabolic waste products in a dissolved form. In some conditions, certain waste products, minerals in particular, may precipitate and form crystals. If these crystals persist for enough time in the urine, they can aggregate and form stones. We sometimes define urinary crystals suspended in the urine as microliths, and stones as macroliths.

The prerequisite for the formation of urinary crystals is a urine supersaturated with components of these crystals. A "stable solution" is one in which the physicochemical conditions of the urine do not allow the formation of crystals, while a "metastable solution" is one in which the formation of crystals is possible, however, aggregation is not sufficient to result in the formation of stones. Lastly, a solution that allows the formation of stones is termed an "unstable solution".

Numerous physical and chemical factors predisposing the patient to the formation of urinary stones have been identified. These factors differ depending on the type of crystals. One factor common to the formation of all types of stones is the urinary concentration. The less concentrated the urine, the less it is saturated in elements responsible for formation of crystals, significantly reducing the chance of stone formation. Thus, increasing the consumption of water in order to promote diuresis will be common to all strategies for prevention of stones, regardless of their type. The majority of dry foods designed for the prevention or dissolution of urinary stones have an increased level of sodium, in order to promote water intake and diuresis.

The concept of relative supersaturation (RSS), developed in human urology in the 1960s and adapted for companion animals, has allowed improvements in the design of foods intended for the prevention and dissolution of urinary stones. RSS is an *in vitro* method based on the determination of the urinary pH and of the urinary concentrations of different analytes involved in the formation of stones. These include calcium, oxalate, sodium, potassium, magnesium, urate, ammonium, citrate, phosphate and pyrophosphate. All these data are analysed by a computer programme that calculates the concentration of a great number of complexes formed by the interaction of different ions present in the urine at a given pH. A RSS is specific to one type of urinary crystal, and RSS values have been determined under which the prevention or even the dissolution of urinary stones is possible. For example, $RSS_{struvite} < 1$ corresponds to an undersaturated urine and is compatible with the prevention and even the dissolution of this type of stone.

2/ Struvite stones

Struvites **(Figure 1)**, also known as magnesium ammonium phosphate stones, are one of the two types of stones most frequently diagnosed in dogs and cats (the other one being calcium oxalate). As their name implies, they result from the crystallisation of ammonium, phosphate and magnesium ions. The components of these stones are present in normal urine, but the formation of crystals **(Figure 2)** depends on factors able to alter the concentration of these different ions and the urinary pH.

Figure 1. Struvite stones.

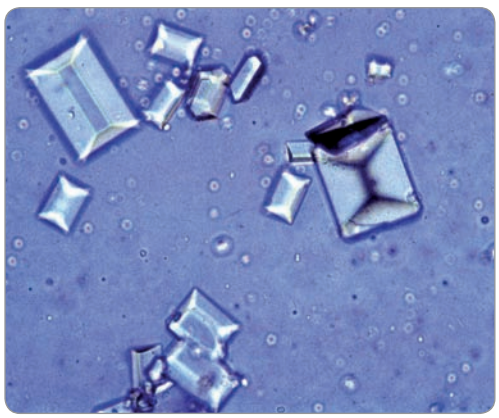


Figure 2. Struvite crystals. Note the typical "coffin" shaped appearance.

The mechanism for formation of struvite crystals differs between dogs and cats. In dogs, the great majority of struvites are formed secondary to a urinary tract infection with urease-producing bacteria, whilst in cats, they develop in a sterile urine in most cases. Urine pH plays an important role in the solubility of struvite crystals. Indeed, it has been shown that, in concentrated urine, an acidic pH (< 6.5) allows the dissolution of struvite crystals whilst an alkaline pH (> 7) promotes their formation (Lulich, 2011).

In dogs as well as in cats, the proportion of struvite stones submitted for spectrophotometric analysis has markedly decreased over the last three decades.

The decline was especially observed in the 1980s and beginning of the 1990s. At the beginning of the 1980s, almost 80% of stones submitted for analysis were struvites. The reduction in the number of struvites occurred simultaneously with the increase in calcium oxalate stones in both species. Since the 2000s, the proportion of struvite stones amongst all stones submitted for analysis has varied between 40% and 50% in both dogs and cats (Osborne, 2009). The development and improvement of foods designed for the prevention and dissolution of struvite stones has probably played a role in this phenomenon.

Struvite stones are radio-opaque. A 2% risk of false-negative results was reported using radiography without contrast. This can be explained by the fact that stones measuring less than 3 mm in diameter can be undetected by conventional radiography. Generally, ultrasound or double contrast cystography are more sensitive than conventional radiography for diagnosing urinary stones (Feeney, 1999). A study in dogs showed that conventional radiography was useful for predicting the type of stone present in the urinary tract. Stones with pyramidal shape, larger than 10 mm, with an ovoid shape and having smooth contours had positive predictive values of 90%, 100%, 80% and 75% for a diagnosis of struvite (Feeney, 1999).

A) Struvites in dogs

In dogs, despite physical and chemical parameters favouring the formation of struvite crystals, the development of this type of stone is unlikely without the presence in the urine of the urease enzyme, produced by some bacteria. The bacteria most commonly reported in association with struvite stones are *Staphylococcus pseudointermedius* and *Proteus spp.* Bacteria which sometimes produce urease and often found in association with struvite stones in dogs include *Escherichia coli*, *Pseudomonas spp.* and *Klebsiella spp.* (Palma, 2013). The role of urease is to convert urea into ammonia. The ammonia produced during this reaction acts as a buffer for the protons present in the urine causing production of ammonium ions. The latter may then react with magnesium and phosphate ions, allowing the formation of struvite crystals. The buffering effect of ammonia is also responsible for an increase in urinary pH, promoting crystallogenesis.

Cases of struvite stones associated with bacteria not producing the urease enzyme and cases of sterile struvites have rarely been reported in dogs. The mechanism of formation in these cases is not well understood and may be similar to the one in cats.

In dogs, struvite stones are more frequently diagnosed in females than in males. This can be explained by a higher risk of urinary infection in female dogs. In dogs, around 95% of struvite stones are discovered in the lower urinary tract, and only 5% in the upper urinary tract (renal pelvis and ureters). Around one third of stones in the upper urinary tract in dogs are struvites.

B) Struvites in cats

Unlike in dogs, struvite stones in cats are formed in sterile urine in approximately 95% of cases. Thus, in the large majority of cases, the formation of struvite stones is only influenced by the urine's physicochemical factors such as the urinary pH, urinary concentration and the concentration of calculogenic minerals such as magnesium and phosphorus (Hostutler, 2005). Increased fibre consumption may also play a role in the formation of struvite stones in cats (Lekcharoensuk, 2001).

A sexual predisposition has not been shown in cats. One epidemiological study showed a higher risk (odds ratio > 2) for several breeds such as Chartreux, Ragdoll, Himalayan and the Domestic Shorthair and a lower risk (odds ratio < 0.5) for Abyssinian, Birman, Russian Blue, Rex, Siamese and cross-bred cats (Thumchai, 1996).

Cats of all ages may be affected. One study, however, showed a higher incidence in cats between 4 and 7 years, with a median age for affected cats of 5.75 years. The rare cases of struvites associated with a urinary infection were more frequent in cats younger than 1 year or older than 10 years (Thumchai, 1996).

C) Treatment of struvite stones

Treatment options for struvite stones include dissolution and ablation. In all cases, once the stones are eliminated, preventative measures will need to be taken in order to prevent recurrence.

Techniques for ablation of urinary stones

Different techniques, more or less invasive, for ablation of urinary stones have been described. These techniques are valid regardless of the nature of the urinary stone.

Voiding urohydropropulsion may be considered in dogs and cats for elimination of stones sufficiently small in size. Small struvite stones are particularly amenable to this technique because their contours are generally smooth, reducing the chance of injuring the urethra during their passage. As a general rule, this technique may be attempted for stones less than 5 mm in diameter in male or female dogs weighing over 8 kg, those less than 3 mm in small dogs or female cats and those less than 1 mm in male cats. In order to obtain maximal relaxation of the urethra, deep sedation or general anaesthesia are recommended.

Laser lithotripsy is used in some institutions for non-invasive ablation of bladder stones. For this, an endoscope brings the fibre laser into contact with the stone in order to fragment it into pieces sufficiently small to be evacuated by urination or using an endoscopic basket. Extracorporeal shockwave lithotripsy is often used for the elimination of kidney stones in human medicine, but at the moment, it is used very infrequently in veterinary medicine due to equipment availability.

Surgical techniques for stone removal include cystotomy and antepubic cystoscopy in the case of bladder stones, and ureterotomy, nephrotomy and nephroscopy in the case of stones located in the upper urinary tract.

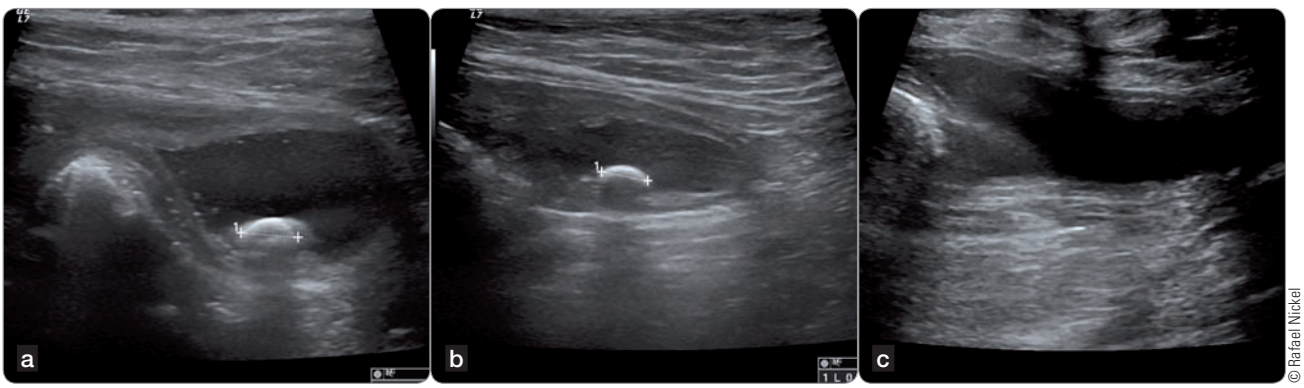
Dissolution of struvite stones

Factors influencing the decision to initiate a dissolution protocol rather than mechanically remove suspected struvite stones are presented in **Table 1**.

The dissolution therapy differs between cats and dogs. Indeed, in the latter, in which stones are due to a urinary tract infection in the majority of cases, elimination of the infection through appropriate antibiotic therapy

Example of successful dissolution of a struvite stone in a dog

Ultrasonography of the urinary tract of a 5-year-old female spayed Poodle before **(a)**, 2 weeks **(b)** and 8 weeks **(c)** after starting a dissolution protocol for a suspected struvite stone. A urinary tract infection with *Staphylococcus pseudointermedius* was diagnosed based on urine culture. Treatment with amoxicillin/clavulanic acid was initiated based on sensitivity to antimicrobials, in combination with a commercial diet designed for dissolution of struvite stones. The significant reduction in the size of the stone (from 0,65 cm to 0,54 cm) on recheck after 2 weeks confirmed the efficacy of treatment. After 8 weeks, the stone had completely disappeared.



is the most important part of the dissolution process. The choice of antibiotic should be based on urine culture and sensitivity, and should be continued for approximately one month after the elimination of the stones in order to avoid recurrence.

As they dissolve, the stones can release bacteria. Urine cultures every four weeks during the dissolution process and approximately one to two weeks after the end of the antibiotic treatment are recommended to ensure the absence of bacterial resistance and to confirm complete elimination of the infection.

In both species, a food specifically designed for the dissolution of struvite stones is recommended. The goal of calculolytic food is to reduce urinary pH, reduce the intake of calculogenic minerals, reduce the urine concentration and, for dogs only, reduce production of urea as a substrate of bacterial urease.

Acidification of the urine increases solubility of struvite crystals. Achieving an acidic urine pH is considered a key element in the success of treatment. In dogs, if a sufficiently acidic urinary pH (< 6.5) is not obtained using a specific diet only, the administration of DL-methionine may be considered at 100 mg/kg BW twice daily. This medication must be used cautiously in cats due to the associated risk of haemolytic anaemia.

Table 1. Factors influencing the decision to initiate a dissolution protocol rather than mechanically remove suspected struvite stones.

Female gender (dogs only)
Struvite crystals in urine sediment
Evidence of urinary tract infection (dogs only)
Previous episode of struvite urolithiasis
Stones having a typical ovoid or pyramidal shape with smooth contours on radiographs
Patient at risk for general anaesthesia

In dogs, a diet reduced in protein ensures a reduction in the production of urea available as substrate for the bacterial urease, which can decrease the production of ammonia. Foods designed for the dissolution of struvite stones are likewise low in magnesium, the intake of this mineral in excessive quantities in the diet having been clearly identified as a factor predisposing to struvite stones in cats (Lekcharoensuk, 2001). Increased levels of sodium in these types of foods stimulate water intake, increasing diuresis and reducing urinary concentration. The result is a reduction in urine saturation of calculogenic minerals.

In dogs, the average duration of the dissolution process is 3 months (Adams and Syme, 2010). In cats, it has recently been shown that a diet formulated with $RSS_{struvite}$ < 1 allowed a dissolution of stones within an average time of 18 days (10-55) (Houston, 2011). The duration of treatment depends in large part on the initial size of the stone and owners' compliance.

Imaging of the urinary tract (radiographs or ultrasound) is recommended at least every 4 weeks during the dissolution protocol to ensure its efficacy. When radiography is used as a follow-up technique, it is recommended to continue the medical treatment for at least one month after confirmation of the absence of mineralized material in the urinary tract as stones cannot be detected accurately using this imaging modality when their size is smaller than 3 mm.

After a successful dissolution protocol for struvite stones, a diet designed for the prevention of relapse is recommended. In dogs, it is also very important to monitor carefully for signs of relapse of urinary tract infection which, without early recognition and treatment, could rapidly lead to recurrence of struvites in predisposed individuals.

3/ Calcium oxalate stones

A) Epidemiological data

Today, calcium oxalate stones **(Figure 3)** are encountered with a frequency similar to that of struvite stones, and represent 40% to 50% of stones submitted for analysis in both dogs and cats (Osborne, 2009).

These stones are more frequently found in males than in females, with a ratio of 2:1 in dogs and 1.5:1 in cats (Gisselman, 2009). This sexual predisposition is also present in humans. A protective role of oestrogens, through reduction in urinary oxalate excretion and increase in urinary citrate excretion, has been suggested. A higher risk of developing these kinds of stones has likewise been identified in sterilised individuals and obese individuals (Lekcharoensuk, 2000; Houston, 2003). Certain canine and feline breeds are predisposed to calcium oxalate stones and are listed in **Table 2**.

Calcium oxalate stones are mainly found in the lower urinary tract in dogs and cats, and only 2% to 3% are located in the renal pelvis or ureter (Gisselman, 2009). Kidney and ureteral stones are composed of calcium oxalate in about one-third of cases in dogs and in almost all cases in cats (Ross, 1999). A large number of cats diagnosed with calcium oxalate stones in the upper urinary tract are also diagnosed with chronic kidney disease. It is likely that repeated, bilateral renal obstructions or sub-obstructions are the cause for renal damage in these individuals. Similarly to struvite stones, calcium oxalate stones are systematically radio-opaque, making their detection possible by conventional radiography.

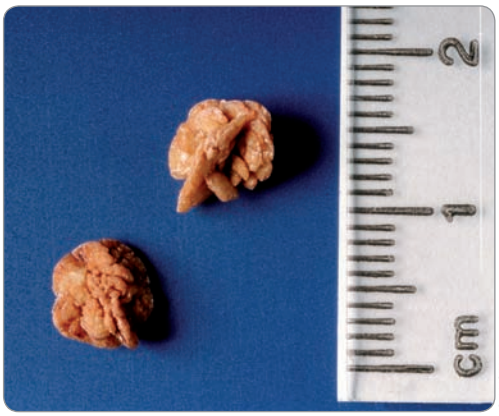


Figure 3. Calcium oxalate stones.

B) Pathophysiology

As their name implies, these stones are formed through crystallisation of calcium and oxalate. The reason why certain animals are prone to developing them is still not well understood. However, hypercalciuria, hyperoxaluria and a persistent high urinary concentration are considered as risk factors.

Table 2. Breeds predisposed to calcium oxalate stones (Odds Ratio (OR) shown in brackets).

Dogs*	Cats*
Standard Schnauzer (OR: 18.06)	Ragdoll
Miniature Schnauzer (OR: 14.10)	British Shorthair
Lhasa Apso (OR: 10.95)	Foreign Shorthair
Parson Russell Terrier (OR: 9.85)	Havana
Papillon (OR: 9.85)	Scottish Fold
Yorkshire Terrier (OR: 6.64)	Persian
Bichon Frise (OR: 6.57)	Himalayan
Keeshond (OR: 5.47)	Exotic Shorthair
Miniature German Spitz (OR: 4.93)	
Samoyed (OR: 4.69)	
Shih Tzu (OR: 4.49)	
Chihuahua (3.88)	
Cairn Terrier (OR: 3.69)	
Maltese Bichon (OR: 3.69)	
Miniature Poodle (OR: 3.32)	
West Highland White Terrier (OR: 3.28)	
Dachshund (OR: 2.69)	

*Lekcharoensuk, Lulich, *et al.* 2000

Hypercalciuria may result from an increase in intestinal absorption of calcium, from increases in its bone resorption or from decreased renal reabsorption. A digestive hyperabsorption has been described in Miniature Schnauzers suffering from calcium oxalate stones (Lulich, 1991). Primary hyperparathyroidism is a cause of hypercalcemia and hypercalciuria through increased bone resorption of calcium and is frequently associated with the formation of calcium oxalates in dogs. Hyperadrenocorticism may likewise contribute to the formation of calcium oxalates through an increase in calciuresis (Feldman and Nelson, 2004).

The development of calcium oxalate stones may also result from a deficit in substances which normally inhibit their formation. Pyrophosphate excreted in the urine is a natural inhibitor of precipitation of calcium oxalate. Pyrophosphate is derived from phosphate, and a restriction in phosphate, sometimes considered to limit the risk of struvite formation, is thought to be a risk factor for the formation of calcium oxalates. Excessive restriction in magnesium may likewise play a role in the formation of oxalate stones. This mineral may effectively complex with oxalate, reducing the latter's capacity to react with calcium for the formation of crystals. Lastly, nephrocalcin is a substance naturally present in urine that inhibits the formation of calcium oxalate crystals. Its activity may be decreased in patients predisposed to these types of stones (Carvalho, 2006).

Contrary to struvites, the solubility of calcium oxalate crystals **(Figure 4)** is not influenced by the urinary pH. Acidosis and aciduria, however, may contribute to formation of this type of stone through an increase in calciuresis and a reduction in urinary excretion of citrate, a competitive inhibitor of the formation of calcium oxalate crystals.

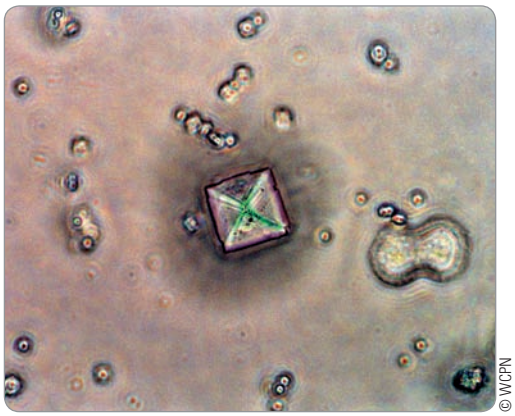


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Figure 4. Dihydrate calcium oxalate crystals. Note the typical "envelope" shape.

C) Treatment and prevention

Calcium oxalate stones cannot be dissolved, and the only treatment option consists of their ablation using the above-mentioned techniques.

It was shown that the recurrence rate in the three years following ablation of calcium oxalate stones was around 50% (Lulich, 1999). The implementation of preventative measures in order to reduce the risk of relapse is thus vital for this type of stones. Diets rich in fat, phosphorus, potassium and magnesium have shown a benefit for the prevention of calcium oxalate stones. A reduction in carbohydrate intake has shown a benefit in dogs but not in cats (Lekcharoensuk, 2002a; Lekcharoensuk, 2002b). The key element in the prevention of calcium oxalate stones is increasing water intake in order to reduce urine concentration. This can be achieved by using a wet food or by adding water to dry foods. It is recommended to obtain a urinary specific gravity lower than 1.035-1.040 in cats and 1.020 in dogs in order to reduce the risk of relapse. Repeating urinalysis regularly allows confirmation that this objective is achieved. Regular urinalyses are also important to confirm the absence of calcium oxalate crystalluria.

When dietary measures are not sufficient to ensure adequate dilution of the urine, the administration of a thiazide diuretic should be considered. This type of diuretic works by inhibition of sodium reabsorption in the distal tubule, which has the consequence of increasing the renal reabsorption of calcium. As a result, the urine becomes less concentrated and the urine calcium concentration is reduced. In dogs, a significant reduction in urinary concentration of calcium has been shown with the use of hydrochlorothiazide at 2 mg/kg BW every 12 hours (Lulich, 2001). Furosemide and other loop diuretics are contraindicated for the prevention of calcium oxalate stones because they increase calciuresis.

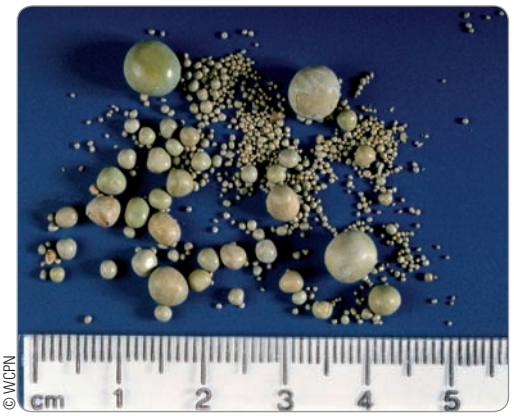

Figure 5. Ammonium urate stones.

Utrasound or radiographs of the urinary tract are recommended at 2 to 4 weeks, 3 months and then at least twice a year after the ablation of the calcium oxalate stones. The goal of these regular rechecks is to detect stones when they are small enough to be extracted by voiding urohydropropulsion rather than with the use of more invasive or expensive techniques.

4/ Ammonium urate stones

Ammonium urate stones **(Figure 5)** are the third most frequent type of stone encountered in dogs and cats, representing 5 to 10% of stones submitted for analysis in both species. This frequency has not changed over past decades, unlike that for struvite and calcium oxalate.

Urate is a product of the degradation of purines coming from the metabolism of proteins and nucleic acids **(Figure 6)**. Under normal conditions, uric acid is converted into allantoin in the liver under the action of the enzyme uricase, and only a small quantity of uric acid is excreted in the urine. Allantoin is very soluble in the urine, whilst uric acid may complex with different cations, especially ammonium ions, to form ammonium urate crystals **(Figure 7)**.

The large majority of urate stones are found in the lower urinary tract. These stones are radiolucent or only slightly radio-opaque, making the use of ultrasound or double contrast radiography necessary for their detection.

A) Dalmatians

A recessive autosomal genetic mutation exists in Dalmatians responsible for a strong predisposition to urate stones. All Dalmatians are homozygotes for this mutation (Adams and Syme, 2010). These dogs produce hepatic uricase normally, but cannot ensure the transport of uric acid into the hepatocytes for its conversion into allantoin and into the renal proximal tubule cells for its reabsorption. This results in hyperuricosuria, causing formation of urate crystals.

In more than 90% of cases, the urate stones submitted for analysis are from male individuals. It is likely that the smaller diameter of the urethra in male dogs make them more prone to urinary obstructions than females, justifying the ablation of stones and their submission for analysis more frequently in males than in females. The prevalence of urate stones in male Dalmatians is estimated at approximately 30% (Bannasch, 2004).

The genetic mutation responsible for the formation of urate stones in Dalmatians has also been identified in English Bulldogs and Black Russian Terriers. The frequency of the mutation is, however, much lower in these two breeds than in Dalmatians.

B) Hepatic dysfunction

Hepatic dysfunction predisposes to urate stones through decreased hepatic conversion of uric acid into allantoin, causing hyperuricosuria. The hepatic dysfunction may likewise be responsible for reduction in the conversion of urea into ammonia, causing hyperammoniuria. Even if, theoretically, all forms of hepatic insufficiency should predispose patients to urate stones, the latter are most often encountered in association with a portosystemic shunt.

C) Treatment and prevention

Ammonium urate stones may be dissolved with adapted therapy. The treatment consists of a diet low in protein, alkalisation of the urine and administration of a xanthine oxidase inhibitor. The purpose of restricting protein is to reduce the quantity of purines causing the formation of

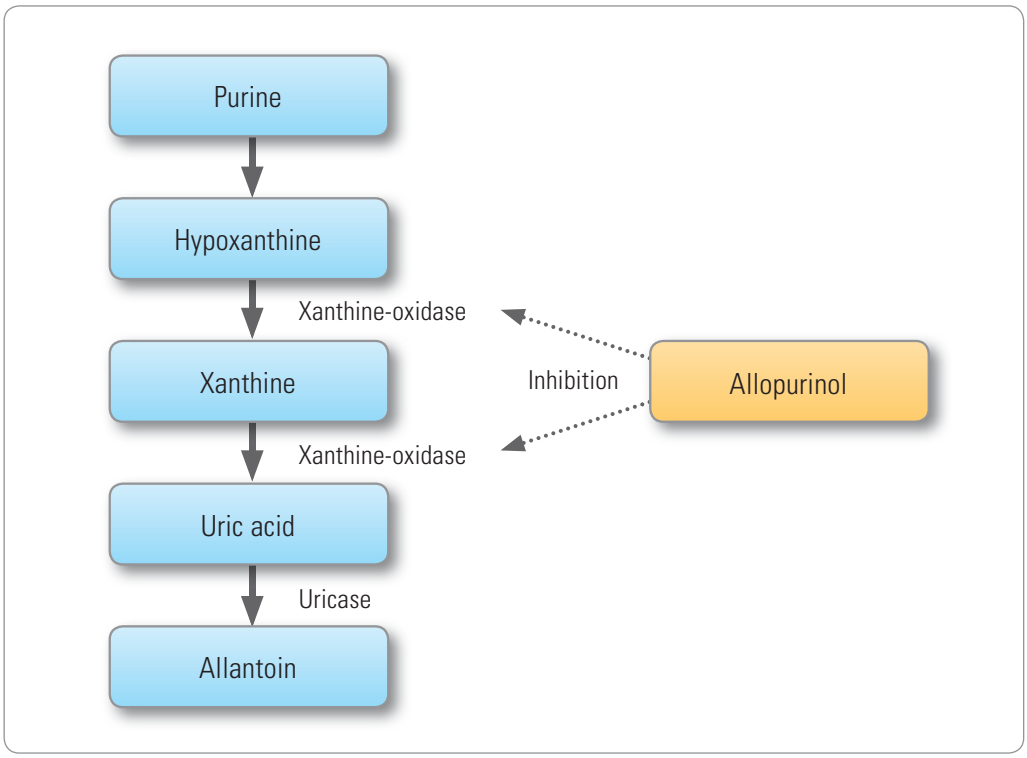

Figure 6. Metabolism of purines. Allopurinol reduces the formation of uric acid by inhibition of the xanthine oxidase enzyme.

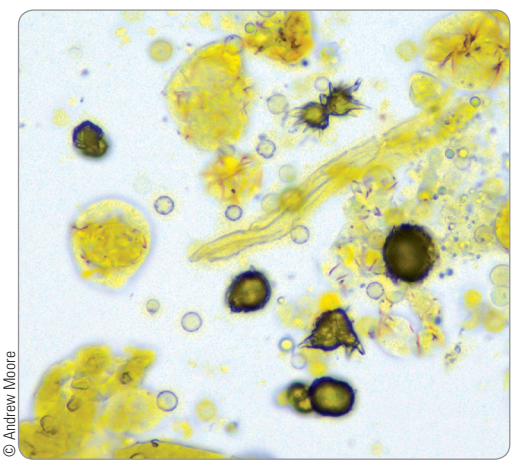

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Figure 7. Urate crystals. Note the spherical shape and yellow-brown colour of these crystals. The detection of urate crystals in the urine of non-Dalmatian dogs should raise the suspicion of hepatic dysfunction.

uric acid. Today, it is possible to reduce the level of purine in a diet without reducing the level of protein.

The solubility of urate crystals is lower at an acidic pH. Diets designed for the dissolution or prevention of urate stones aim to obtain a slightly alkaline urinary pH: between 7 and 7.5. If a slightly alkaline pH is not obtained with the use of a diet alone, potassium citrate may be considered as an alkalinising agent, at an initial dose of 50 mg/kg BW twice a day.

Allopurinol, an inhibitor of the xanthine oxidase enzyme is used at a dose of 15 mg/kg BW twice daily during the dissolution process in order to decrease the production of uric acid. It is important to use allopurinol only in combination with a low-purine diet as an excess of purine precursors in this situation could increase the risk of xanthine stone formation. Allopurinol is metabolised by the liver and therefore, is not recommended in patients suffering from a

portosystemic shunt because prolonged elimination can significantly increase the risk of xanthine stone formation.

On average, urate stones are dissolved in 3.5 months using a combination of dietary modification, alkalinisation of the urinary pH and treatment with a xanthine oxidase inhibitor (Bartges, 1999). Follow-up by ultrasonography or double contrast radiography is recommended every 4 weeks in order to ensure the efficacy of the dissolution treatment. If, after 8 weeks of treatment, the size of the stones has not decreased, the diagnosis should be re-evaluated and an alternative therapeutic strategy implemented.

In patients suffering from a portosystemic shunt, correction of the shunt and restoration of adequate hepatic function may be associated with spontaneous dissolution of urate stones (McCue, 2009).

Once the dissolution (or ablation) of urate stones has been done, it is important to reduce the risk of relapse by feeding a diet reduced in purine and promoting a slightly alkaline urinary pH. In the event of relapse despite the modified diet, long-term therapy with allopurinol should be considered. Regular follow-up on the urinary tract by ultrasonography or double contrast cystography is then recommended due to the risk of xanthine stone formation. As for all types of stones, increasing consumption of water in order to obtain less concentrated urine is a key element of the preventative strategy.

D) Urate stones in cats

As for dogs, cats suffering from portosystemic shunts may develop urate stones. The mechanism by which certain cats not suffering from hepatic disease develop urate stones is not understood. Cats of the Siamese breed seem to be predisposed. A sexual predisposition has not been reported (McCue, 2009).

At this time, strategies for dissolution of urate stones have not been established in cats, and surgical ablation of the stones is the option most commonly used. As for dogs, a low-purine diet promoting a slightly alkaline pH, as well as increased water consumption are recommended to prevent recurrence. Diets developed for management of chronic kidney disease, preferably in wet form, are generally adequate for preventing relapse of urate stones in cats.

Detailed knowledge on the mechanisms of formation of the different types of stones is important in order to determine the best treatment option (dissolution or ablation) and implement the most suitable follow-up programme to limit the risks of relapse. In certain cases, the formation of bladder stones is the consequence of a metabolic disease requiring specific management. Numerous veterinary foods are now available allowing the dissolution or prevention of different types of urinary stones in dogs and cats.

5. Urinalysis

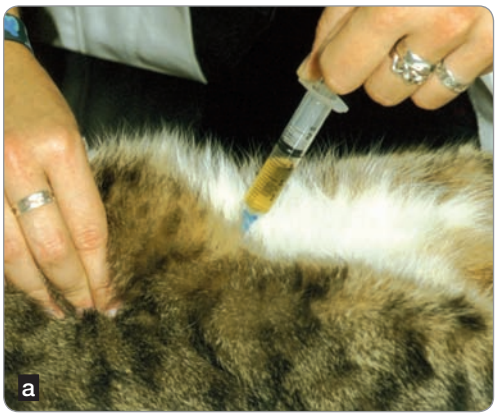
> SUMMARY

Urinalysis is an essential component of investigations of a patient with lower urinary tract disease. Samples can be collected using a variety of methods, although cystocentesis is often the preferred technique. Free catch, midstream and catheter collection are alternative options. Interpretation of test results should include consideration of the collection technique used. The differences in normal canine and feline results will be discussed as well as limitations of some of the available tests.

Urine samples can be collected by cystocentesis, catheter, midstream or free catch methods. Depending on the analysis required, it may be perfectly acceptable to collect and analyse a free catch or midstream sample. Free catch samples may be "contaminated" by cells, protein and bacteria in the urethra/genital tract and litter tray, and this can affect interpretation of some test results. **Table 1** summarises the "ideal" sample requirements, although it is important to emphasise that free catch samples can still be submitted for bacteriology, UPC etc. – it is just that the interpretation may be more complicated.

1/ Cystocentesis urine sample collection

Urine samples can be obtained from conscious cats with minimal restraint. The author prefers to use a one-inch 23 gauge needle and a 5 or 10 mL syringe. The patient is restrained as gently as possible standing, in lateral recumbency or in dorsal recumbency. In general, it is best to have the cat in the position in which it feels most comfortable. If the cat becomes tense, the bladder will be much harder to palpate, so it is in your own interests to keep the cat as calm and happy as possible. The bladder is palpated and stabilised with one hand while the other hand is used to manipulate the syringe. If the cat is lying on his back, the bladder can be pushed caudally so it is stabilised between your hand and the bones of the pelvis **(Figure 1a)**. If the cat is standing or lying on its side, the bladder can be stabilised so that your thumb is at the cranial pole and your fingers gently lift the bladder towards you **(Figure 1b)**. Once the bladder is stabilised, the needle guard should be removed and the needle placed gently onto the skin over the bladder. By resting the needle on the skin before slowly sliding through, most cats will not appear to feel anything and won't be startled. The needle is passed all the way through the skin so that the needle hub is sitting on the skin. The urine is aspirated with one hand and then pressure is released with the other before withdrawing the needle. Adverse effects of cystocentesis are very rare in healthy cats but include bruising and haemorrhage (usually microscopic, but may affect urinalysis results), transient vagal stimulation (retching, panting, collapse), urine leakage and bladder rupture (seen rarely in cats with urethral obstruction). If the bladder is not palpable but cystocentesis is very desirable (for example, when a urine culture is needed) ultrasound can be used to locate the bladder and guide the needle. A good quantity of ultrasound gel is applied to the area before imaging and



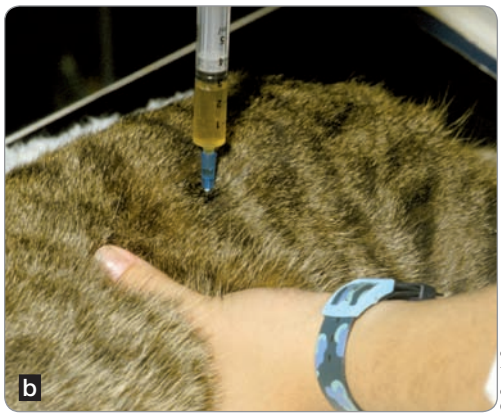


Figure 1. Cystocentesis can be performed in cats in a standing position, dorsal recumbency (a) or lateral recumbency (b).

sampling, taking care not to introduce the needle through the gel or through the tip of the probe!

In dogs, cystocentesis can be performed with the dog standing or in lateral recumbency. It is necessary to locate and immobilize the urinary bladder. Bladder immobilization can be difficult in very large or obese dogs. In these patients, a useful tip is to apply pressure on the abdominal wall with the palm of the hand on the opposite side to which the sample is to be collected. Blind cystocentesis is not recommended; it is generally unsuccessful and can damage a number of different abdominal organs. Gentle agitation of the bladder via abdominal palpation may enhance the recovery of material that may have gravitated to the dependent portions of the bladder. The author normally uses a 22G needle, 1.5-3 inches long, depending on the size of the dog. The needle is inserted through the ventral abdominal wall and advanced to the caudoventral aspect of the bladder. The urine is gently aspirated into the syringe. It is important not to apply excessive pressure against the bladder because it can result in leakage of urine into the abdominal cavity. As in cats, if the bladder cannot be located or the clinician is not confident with the procedure, an ultrasound-guided cystocentesis will simplify the urine collection.

2/ Free catch urine sample collection

To collect a free catch sample from a cat, the patient is confined with an empty litter tray or one containing non-absorbent cat litter (commercial brands include Katkor®, kit4cat®, Mikki®; non commercial options include clean

Table 1. Preferred sample type for analysis.

	Free catch	Midstream (dogs)	Catheter	Cystocentesis
Specific gravity	✓	✓	✓	✓
Dipstick	✓	✓	✓	✓
Bacteriology		(✓)	(✓)	✓
Protein to creatinine ratio*		(✓)	(✓)	✓
Sediment		(✓)	(✓)	✓

* Urine sediment should be examined before performing UPC to rule out post-renal conditions.

Figure 2. Free catch urine collection is helpful for initial urinalysis, although this is not the preferred method of collection when assessing sediment, bacteriology or proteinuria.

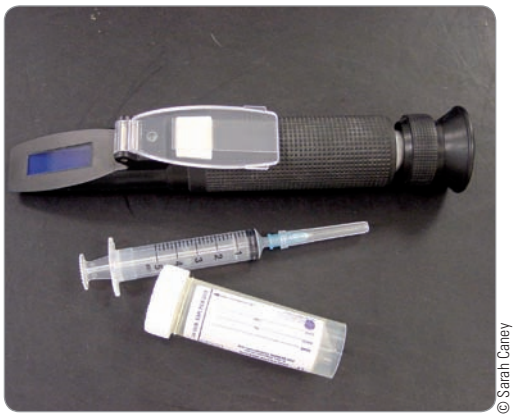


Figure 3. Urine specific gravity should be assessed using a refractometer and not urine dipsticks.

aquarium gravel or chopped up plastic bags). Once the cat has urinated, a urine sample is collected using a pipette or syringe and placed into a sterile tube for subsequent analysis **(Figure 2)**. The sample should be analysed as soon as possible. If immediate analysis is not possible, the sample should be refrigerated.

When normal voiding samples are obtained in dogs, the first portion of the urine stream is discarded, and a "mid-stream" sample is used for urinalysis. Although manual compression of the bladder can induce micturition in some situations, this technique can have several detrimental effects on the patient and on the quality of the obtained samples, so the authors don't recommend it.

3/ Catheter sampling

In cats, collection of a urine sample by this technique is reserved for those cases where catheterisation is required for other diagnostic or therapeutic reasons such as treatment of urethral obstruction or performing a retrograde contrast study.

Urinary catheterization can induce trauma and bacterial urinary tract infection. Thus, it is important to avoid unnecessary catheterization and to perform the procedure using an atraumatic and aseptic technique. Catheters with a diameter ranging between 4-10 Fr are valid for the majority of dogs, but the clinician should try to use the smallest diameter catheter that will facilitate the catheterization.

4/ In-house urinalysis

Whenever possible, routine urinalysis should be performed in-house, to avoid the possibility of inaccurate results as a consequence of delayed analysis when samples are sent to an external laboratory.

Gross examination and specific gravity

Urine should be observed and its colour, clarity and presence of gross contamination determined. The specific gravity (USG) should be assessed using a refractometer **(Figure 3)**. Urine may be defined as isosthenuric (USG = 1.007-1.012 same as glomerular filtrate), hyposthenuric (USG < 1.007) or hypersthenuric (USG > 1.012).

Urine dipsticks are unreliable for assessment of USG, nitrite, urobilinogen and leucocytes in cats and dogs. A 5 mL urine sample can be centrifuged, and the sediment stained and examined by light microscopy. Normal findings are summarised in **Table 2**.

Table 2. In-house urinalysis and interpretation.

Parameter	Normal findings	Comment
Specific gravity (USG)	Usually 1.040-1.060 (cats) 1.015-1.045 (dogs)	Always assess using a refractometer and not a dipstick! USG can be reduced by physiological causes (*e.g.*, eating a liquid diet), iatrogenic causes (*e.g.*, furosemide treatment) and pathological causes (*e.g.*, chronic kidney disease). USG can be increased by heavy glucosuria, heavy proteinuria and presence of radiographic contrast material.
Dipstick	Glucose: negative	A positive reading for glucose on a dipstick indicates glucosuria due to either stress, diabetes mellitus, hyperglycaemia due to receiving glucose-containing intravenous fluids or, rarely, renal tubular disease.
	Ketones: negative	A positive reading can be found in some cats with diabetes mellitus. Occasionally, ketones will be seen in non-diabetic cats which are in a catabolic state.
	Blood: negative	Dipsticks are sensitive in detecting small amounts of red blood cells, haemoglobin and myoglobin – all of which can produce a red discolouration of the urine and positive reaction for blood on dipstick.
	pH: 5.5-7.5	Urine pH may be affected by diet, stress (hyperventilation), acid-base disorders, drugs, renal tubular acidosis and urinary tract infections. pH results should be interpreted carefully; urine with a mildly acidic pH can be measured alkaline by the dipstick. If an accurate pH reading is critical, the clinician should consider using a pH meter or submitting the sample to an external laboratory.
	Protein: negative/trace/1+ reading common in normal cats and dogs	Dipsticks are relatively insensitive in documenting proteinuria and do not take into account the concentration of the urine. The results should therefore be interpreted according to the patient USG (measured using a refractometer and not a dipstick!). The urine protein to creatinine ratio (UPC) is recommended in all cats with known renal disease or where protein assessment is required.
	Bilirubin: negative	In contrast to dogs, bilirubin should not be present in normal cat urine. Trace of mild bilirubinuria (1+ or 2+ [in highly concentrated urine]) could be a normal finding, especially in male dogs.
Sediment	Normal urine should contain: • Less than 10 red blood cells per high power field (x400) • Less than 5 white blood cells per high power field (x400) • Epithelial cells (numbers greater in free catch *vs.* cysto samples) • +/- Struvite crystals (see comment)	According to the method of urine collection (free catch *vs.* cystocentesis): • Presence, type and quantity of epithelial cells may vary. • Neoplastic cells from the bladder, urethra and prostate may be seen. • Micro-organisms should normally not be seen in urine samples but may be present due to contamination of free catch or mid-stream samples. Casts formed from protein and cells in the distal tubule may be identified. A few hyaline (protein) casts are a normal finding, but excessive casts indicate renal disease, and material trapped in casts may indicate the aetiology (*e.g.*, leucocyte casts suggest inflammation/infection, for example due to pyelonephritis). Struvite crystalluria is common in normal cats. Due mainly to a reduction in temperature (and change in pH), an increase in crystalluria due to additional precipitation will often occur after urine is collected. In assessing the significance of crystalluria, it is important to consider the type of crystal and quantity. Urate crystals can be seen in cats with hepatopathies (*e.g.*, portosystemic shunts) and oxalate crystals can be found in hypercalcaemic cats. Heavy crystalluria is a risk factor for urolithiasis and crystal-matrix urethral plug formation. It is important that crystalluria is not over interpreted. In many cases of idiopathic lower urinary tract disease, crystalluria is a normal (incidental) finding.
Urine protein to creatinine (UPC)	Most healthy cats and dogs have a UPC < 0.2, although an upper limit of 0.4-0.5 is usually quoted	Guidelines for patients with chronic kidney disease (IRIS, www.iris-kidney.com) Cats: • < 0.2 – not proteinuric • 0.2-0.4 – borderline proteinuria • > 0.4 – proteinuria Dogs: • < 0.2 – not proteinuric • 0.2-0.5 - borderline proteinuria • > 0.5 - proteinuria

References

Chapter 1

Bartges JW, Finco DR, Polzin DJ, *et al.* Pathophysiology of urethral obstruction. *Vet Clin North Am Small Anim Pract* 1996;26:255.

Bradley AM, Lappin MR. Intravesical glycosaminoglycans for obstructive feline idiopathic cystitis: a pilot study. *J Feline Med Surg* 2013;E-pub ahead of print.

Cooper ES, Owens TJ, Chew DJ, *et al.* A protocol for managing urethral obstruction in male cats without urethral catheterization. *J Am Vet Med Assoc* 2010;237:1261-1266.

Corgozinho KB, de Souza HJ, Pereira AN, *et al.* Catheter-induced urethral trauma in cats with urethral obstruction. *J Feline Med Surg* 2007;9:481-486.

Eisenberg BW, Waldrop JE, Allen SE, *et al.* Evaluation of risk factors associated with recurrent obstruction in cats treated medically for urethral obstruction. *J Am Vet Med Assoc* 2013; 243:1140-1146.

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.

Fults M, Herold LV. Retrospective evaluation of presenting temperature of urethral obstructed male cats and the association with severity of azotemia and length of hospitalization: 243 cats (2006-2009). *J Vet Emerg Crit Care* (San Antonio) 2012;22:347-354.

Galluzzi F, De Rensis F, Menozzi A, *et al.* Effect of intraurethral administration of atracurium besylate in male cats with urethral plugs. *J Small Anim Pract* 2012; 53: 411-415.

Gerber B, Eichenberger S, Reusch CE. Guarded-long term prognosis in male cats with urethral obstruction. *J Feline Med Surg* 2008;10:16-23.

Hetrick PF, 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.

Holmes ES, Weisse C, Berent AC. Use of fluoroscopically guided percutaneous antegrade urethral catheterization for the treatment of urethral obstruction in male cats: 9 cases (2000-2009). *J Am Vet Med Assoc* 2012;241:603-607.

Kruger JM, Osoborne CA, Ulrich LK. Cystocentesis. Diagnostic and therapeutic considerations. *Vet Clin North Am Small Anim Pract* 1996;26:353-361.

Lefevre-Borg F, O'Connor SE, Schoemaker H, *et al.* Alfuzosin, a selective alpha 1-adrenoceptor antagonist in the lower urinary tract. *Br J Pharmacol* 1993;109:1282-1289.

Lekcharoensuk C, Osborne CA, Lulich JP. Evaluation of trends in frequency of urethrostomy for treatment of urethral obstruction in cats. *J Am Vet Med Assoc* 2002;221:502-505.

Meige F, Sarrau S, Autefage A. Management of traumatic urethral rupture in 11 cats using primary alignment with a urethral catheter. *Vet Comp Orthop Traumatol* 2008;21:76-84.

Nickel RF. Perineal urethrostomy. In: Van Sluijs FJ. Atlas of Small Animal Surgery. Uitgeverij Bunge, Utrecht, 1992;161-162.

Nickel RF. Complicaties na perineale urethrostomie bij de kater. *Tijdschr Diergeneesk* 1995;21:632-634.

Nickel RF, Peppler C. Chirurgische Erkrankungen der Harnröhre. In: Bonath KH, Kramer M. Kleintierkrankheiten - Chirurgie der Weichteile. 2. Auflage, Verlag Eugen Ulmer Stuttgart, 2014;295-307.

O'Hearn AK, Wright BD. Coccygeal epidural with local anesthetic for catheterization and pain management in the treatment of feline urethral obstruction. *J Vet Emerg Crit Care* (San Antonio) 2011;21:50-52.

Ramage AG, Wyllie MG. A comparison of the effects of doxazosin and terazosin on the spontaneous sympathic drive to the bladder and related organs in anaesthetized cats. *Eur J Pharmacol* 1995;294:645-650.

Ruda L, Heiene R. Short- and long-term outcome after perineal urethrostomy in 86 cats with feline lower urinary tract disease. *J Small Anim Pract* 2012;53:693-698.

Saevik BK, Trangerud C, Ottesen N, *et al.* Causes of lower urinary tract disease in Norwegian cats. *J Feline Med Surg* 2011;13:410-417.

Scrivani PV, Chew DJ, Buffington CA, *et al.* Results of retrograde urethrography in cats with idiopathic, non-obstructive lower urinary tract disease and their association with pathogenesis: 53 cases (1993-1995). *J Am Vet Med Assoc* 1997;211:741-748.

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.

Tacke SP, Bonath KH. Anästhesie, Schmerztherapie. In: Bonath KH, Kramer M. Kleintierkrankheiten - Chirurgie der Weichteile. 2. Auflage, Verlag Eugen Ulmer Stuttgart, 2014;642-660.

Zezza L, Reusch CE, Gerber B. Intravesical application of lidocaine and sodium bicarbonate in the treatment of obstructive idiopathic lower urinary tract disease in cats. *J Vet Intern Med* 2012;26:536-531.

Chapter 2

Bartges JW. What's new in feline LUTD? ECVIM Congress, Munich, Germany 2002.

Beata C, Beaumont-Graff E, Coll V, *et al.* Effect of alpha-casozepine (Zylkene) on anxiety in cats. *J Vet Behav* 2007;2:40-46.

Buffington CAT, Westropp JL, Chew DJ, *et al.* Risk factors associated with clinical signs of lower urinary tract disease in indoor-housed cats. *J Am Vet Med Assoc* 2006;228:722-725.

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.

Buffington CAT. Idiopathic cystitis in domestic cats – beyond the lower urinary tract. *J Vet Intern Med* 2011;25:784-796.

Caney S, Gunn-Moore D. Caring for a cat with lower urinary tract disease. Cat Professional 2011.

Chew DJ, Bartges JW, Adams LG, *et al.* Randomized placebo-controlled clinicial trial of pentosan polysulfate sodium for treatment of feline interstitial (idiopathic) cystitis. ACVIM Forum, Montreal, Quebec. *JVIM* 2009:674.

Gunn-Moore DA, Cameron ME. A pilot study using synthetic feline facial pheromone for the management of feline idiopathic cystitis. J *Feline Med Surg* 2004;6(3):133-138.

Gunn-Moore DA, Shenoy CM. Oral glucosamine and the management of feline idiopathic cystitis. *J Feline Med Surg* 2004;6:219-225.

King JN, Steffan J, Heath SE, *et al.* Determination of the dosage of clomipramine for the treatment of urine spraying in cats. *J Am Vet Med Assoc* 2004;225:881-887.

Kraijer M, Fink-Gremmels J, Nickel RF. The short-term clinical efficacy of amitriptyline in the management of idiopathic feline lower urinary tract disease: a controlled clinical study. *J Feline Med Surg* 2003;5:191-196.

Kruger JM, Conway TS, Kaneene JB, *et al.* Randomized controlled trial of the efficacy of short-term amitriptyline administration for the treatment of acute, nonobstructive, idiopathic lower urinary tract disease in cats. *J Am Vet Med Assoc* 2003;222:749-58.

Landsberg GM, Wilson AL. Effects of clomipramine on cats presented for urine marking. *J Am Anim Hosp Assoc* 2005;41:3-11.

Markwell PJ, Buffington CA, Chew DJ, *et al.* Clinical evaluation of commercially available urinary acidification diets in the management of idiopathic cystitis in cats. *J Am Vet Med Assoc* 1999;214:361-365.

Osborne CA, Kruger JM, Lulich JP, *et al.* Prednisolone therapy of idiopathic feline lower urinary tract disease: a double-blind clinical study. *Vet Clin North Am Small Anim Pract* 1996;26:563-569.

Stella JL, Lord LL, Buffington CA. Sickness behaviors in response to unusual external events in healthy cats and cats with feline interstitial cystitis. *J Am Vet Med Assoc* 2011;238:67-73.

Chapter 3

Bailiff NL, Nelson RW, Feldman EC, *et al.* Frequency and risk factors for urinary tract infection in cats with diabetes mellitus. *J Vet Intern Med* 2006;20:850-855.

Barsanti JA. Genitourinary infections. In Greene CE, ed. Infectious diseases of the dog and cat. St Louis: Elsevier Saunders Mo, 2012;1013-1031.

Bartges JW, Barsanti JA. Bacterial urinary tract infections in cats. In Bonagura JD, ed. Current Veterinary Therapy XIII. Philadelphia: W.B. Saunders Pa, 2000;80-883.

Bowles, M. Alternative options for managing urinary tract disease in the dog and cat, in *Proceedings*. 30th ACVIM Forum 2012;620-622.

Bubenik LJ, Hosgood GL, Waldron DR, *et al.* Frequency of urinary tract infection in catheterized dogs and comparison of bacterial culture and susceptibility testing results for catheterized and noncatheterized dogs with urinary tract infections. *J Am Vet Med Assoc* 2007;231:893-899.

Chew DJ, Dibartola SP, Schenck P. Cystitis and urethritis: urinary tract infection. In Chew DJ, Dibartola SP, Schenck P eds. Canine and feline nephrology and urology. St Louis: Elsevier Saunders Mo, 2011;40-271.

Cohn LA, Gary AT, Fales WH, *et al.* Trends in fluoroquinolone resistance of bacteria isolated from canine urinary tracts. *J Vet Diag Invest.* 2003;15:338-343.

Forrester SD, Troy GC, Dalton MN, *et al.* Retrospective evaluation of urinary tract infection in 42 dogs with hyperadrenocorticism or diabetes mellitus or both. *J Vet Intern Med* 1999;13:557-560.

Freigtag T, Squires RA, Schmid J, *et al.* Antibiotic sensitivity profiles do not reliably distinguish relapsing or persisting infections from reinfections in cats with chronic renal failure and multiple diagnoses of *Escherichia coli* urinary tract infection. *J Vet Intern Med* 2006;20: 245-249.

Gatoria IS, Saini NS, Rai TS. Comparison of three techniques for the diagnosis of urinary tract infections in dogs with urolithiasis. *J Small Anim Pract* 2006;47:727-732.

Hamaide AJ, Martinez SA, Hauptman J, *et al.* Prospective comparison of four sampling methods (cystocentesis, bladder mucosal swab, bladder mucosal biopsy, and urolith culture) to identify urinary tract infections in dogs with urolithiasis. *J Am Anim Hosp Assoc* 1998;34: 423-430.

Kivistö AK, Vasenius H, Sandholm M. Canine bacteriuria. *J Small Anim Pract* 1977;18:707-712.

Kvitko-White HL, Cook AK, Nabity MB, *et al.* Evaluation of a catalase-based urine test for the detection of urinary tract infection in dogs and cats. *J Vet Intern Med* 2013;27:1379-1384.

Kruger J, Osborne C, Goyal SM, *et al.* Clinical evaluation of cats with lower urinary tract disease. *J Am Vet Med Assoc* 1991;199:211-216.

Kukanich KS. Urinary tract nutraceuticals: critical evaluation of efficacy, in *Proceedings*. 31th ACVIM Forum 2013.

Labato MA. Uncomplicated urinary tract infection. In Bonagura JD, Twedt DC, (eds). Current Veterinary Therapy XIV. St Louis: Saunders Elsevier; Mo, 2009;918-921.

Lees GE. Bacterial urinary tract infections. *Vet Clin North Am Small Anim Pract* 1996;26:297-304.

Litster A, Moss S, Honnery M, *et al.* Prevalence of bacterial species in cats with clinical signs of lower urinary tract disease: recognition of *Staphylococcus felis* as a possible feline urinary tract pathogen. *Vet Microbiol* 2007;121:182-188.

Litster A, Moss S, Platell J, *et al.* Occult bacterial lower urinary tract infections in cats-urinalysis and culture findings. *Vet Microbiol* 2009;136:130-134.

Lulich JP, Osborne CA. Urine culture as a test for cure: why, when and how? *Vet Clin North Am Small Anim Pract* 2004;34:1027-1041.

Masson P, Matheson S, Webster AC, *et al.* Meta-analyses in prevention and treatment of urinary tract infections. *Infect Dis Clin North Am* 2009;23:355-385.

Pressler B. Fungal urinary tract infection. In Bartges J & Polzin DJ eds. Nephrology and Urology of Small Animals. Chichester: Wiley-Blackwell, UK, 2011;717-724.

Senior D. Urinary tract infection-bacterial. In Bartges J & Polzin DJ eds. Nephrology and Urology of Small Animals. Chichester: Wiley-Blackwell, UK, 2011;710-717.

Smee N, Grauer GF, Schermerhorn TF. Investigations into the effect of cranberry extract on bacterial adhesion to canine uroepithelial cells. *J Vet Intern Med* 2011;25:506-512/716-717.

Smee N, Loyd K, Grauer G. UTIs in small animal patients: part 1: etiology and pathogenesis. *J Am Anim Hosp Assoc* 2013;49:1-7.

Swenson CL, Boisvert AM, Gibbons-Burgener SN, *et al.* Evaluation of modified Wright-staining of dried urinary sediment as a method for accurate detection of bacteriuria in cats. *Vet Clin Pathol* 2011;40:256-264.

Tivapasi MT, Hodges J, Byrne BA, *et al.* Diagnostic utility and cost-effectiveness of reflex bacterial culture for the detection of urinary tract infection in dogs with low urine specific gravity. *Vet Clin Pathol* 2009;38:337-342.

Way LI, Sullivan LA, Jhonson V, *et al.* Comparision of routine urinalysis and urine Gram stain for detection of bacteriuria in dogs. *J Vet Emerg Crit Care* 2013;23:23-28.

Weese JS, Blondeau JM, Boothe D, *et al.* Antimicrobial use guidelines for treatment of urinary tract disease in dogs and cats: antimicrobial guidelines working group of the international society for companion animal infectious diseases. *Vet Med Int* 2011;263768.doi: 10.4061/2011/263768.

Westropp JL, Sykes JE, Irom S, *et al.* Evaluation of the efficacy and safety of high dose short duration enrofloxacin treatment regimen for uncomplicated urinary tract infections in dogs. *J Vet Intern Med* 2012;26:506-512.

Chapter 4

Adams LG, Syme HM. Canine ureteral and lower urinary tract diseases. Textbook of Veterinary Internal Medicine (7th Ed). SJ Ettinger and EC Feldman, Saunders-Elsevier 2010;2086-2115.

Bannasch DL, Ling GV, *et al.* Inheritance of urinary calculi in the Dalmatian. *J Vet Intern Med* 2004;18(4):483-487.

Bartges JW, Osborne CA, *et al.* Canine urate urolithiasis. Etiopathogenesis, diagnosis, and management. *Vet Clin North Am Small Anim Pract* 1999;29(1):161-191.

Carvalho M, Lulich JP, *et al.* Defective urinary crystallization inhibition and urinary stone formation. *Int Braz J Urol* 2006;32(3):342-348.

Feeney DA, Weichselbaum RC, *et al.* Imaging canine urocystoliths. Detection and prediction of mineral content. *Vet Clin North Am Small Anim Pract* 1999;29(1):59-72.

Feldman EC, Nelson NC. Canine and Feline Endocrinology and Reproduction (3rd Ed), Saunders 2004.

Gisselman K, Langston C, *et al.* (2009). Calcium oxalate urolithiasis. *Compend Contin Educ Vet* 2009;31(11):496-502.

Hostutler RA, Chew DJ, *et al.* Recent concepts in feline lower urinary tract disease. *Vet Clin North Am Small Anim Pract* 2005;35(1):147-170.

Houston DM, Moore AE, *et al.* Feline urethral plugs and bladder uroliths: a review of 5,484 submissions 1998-2003. *Can Vet J* 2003;44(12):974-977.

Houston DM, Weese HE, *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.

Lekcharoensuk C, Lulich JP, *et al.* Association between patient-related factors and risk of calcium oxalate and magnesium ammonium phosphate urolithiasis in cats. *J Am Vet Med Assoc* 2000;217(4):520-525.

Lekcharoensuk C, Lulich JP, *et al.* Patient and environmental factors associated with calcium oxalate urolithiasis in dogs. *J Am Vet Med Assoc* 2000;217(4):515-519.

Lekcharoensuk C, Osborne CA, *et al.* Epidemiologic study of risk factors for lower urinary tract diseases in cats. *J Am Vet Med Assoc* 2001;218(9):1429-1435.

Lekcharoensuk C, Osborne CA, *et al.* Association between dietary factors and calcium oxalate and magnesium ammonium phosphate urolithiasis in cats. *J Am Vet Med Assoc* 2001;219(9):1228-1237.

Lekcharoensuk C, Osborne CA, *et al.* Associations between dietary factors in canned food and formation of calcium oxalate uroliths in dogs. *Am J Vet Res* 2002;63(2):163-169.

Lekcharoensuk C, Osborne CA, *et al.* Associations between dry dietary factors and canine calcium oxalate uroliths. *Am J Vet Res* 2002;63(3):330-337.

Lulich JP, Osborne CA, *et al.* Canine and feline urolithiasis: diagnosis, treatment and prevention. Nephrology and Urology of Small Animal. JW Bartges and DJ Polzin, Blackwell 2011;687-706.

Lulich JP, Osborne CA, *et al.* Canine calcium oxalate urolithiasis. Case-based applications of therapeutic principles. *Vet Clin North Am Small Anim Pract* 1999;29(1):123-139.

Lulich JP, Osborne CA, *et al.* Effects of hydrochlorothiazide and diet in dogs with calcium oxalate urolithiasis. *J Am Vet Med Assoc* 2001;218(10):1583-1586.

Lulich JP, Osborne CA, *et al.* Prevalence of calcium oxalate uroliths in miniature schnauzers. *Am J Vet Res* 1991;52(10):1579-1582.

McCue J, Langston C, *et al.* Urate urolithiasis. *Compend Contin Educ Vet* 2009;31(10):468-475;quiz 475.

Osborne CA, Lulich JP, *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(1):183-197.

Palma D, Langston C, *et al.* Canine struvite urolithiasis. *Compend Contin Educ Vet* 2013;35(8):E1;quiz E1.

Ross SJ, Osborne CA, *et al.* Canine and feline nephrolithiasis. Epidemiology, detection, and management. *Vet Clin North Am Small Anim Pract* 1999;29(1):231-250.

Thumchai R, Lulich J, *et al.* Epizootiologic evaluation of urolithiasis in cats: 3,498 cases (1982-1992). *J Am Vet Med Assoc* 1996;208(4):547-551.

Chapter 5

Free downloads: technical guides and video guides to cystocentesis and owner collection of urine samples are available on the author's website: http://www.vetprofessionals.com/catprofessional/free_downloads.html

Personal notes

Personal notes

This book has been prepared with the greatest care, taking into account the latest research and scientific discoveries. It is recommended that you refer to the specific regulations of your country. The publisher and authors can in no way be held responsible for any failure of the suggested solutions. Evidence-based medicine has been used throughout this publication wherever possible. Where no evidence base exists, or the available evidence is conflicting or equivocal the authors have provided their collaborative opinion based on their considerable experience and expertise.

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