Veterinary Practice News®
THE INFORMATION LEADER FOR VETERINARY PRACTICE AND BUSINESS

Understanding URINARY TRACT DISEASE

Veterinary
Practice News

veterinarypracticenews.com

GROUP PUBLISHER/CEO
Erik Tolles

EDITORIAL
Editorial Director
Blair Adams
Editor
Jacquie De Almeida
Associate Editor
Samantha Ashenhurst

DESIGN
Alfi Ichwanditio
Azzarine Purwanto
Senior Graphic Designer
Catherine Howlett

VETERINARYPRACTICENEWS.COM
Andrei Kurpatov
Charlie Pang
Hon Mun Mak
Lillian Hu
Rizza Bagnol

AUDIENCE DEVELOPMENT
Eva Pau
Mei Hong
Donna Murray
Sonam Bhardwaj
Camille Garcia
Content and Event Coordinator
Ashley Ward

PRODUCTION
Director of Production and Projects
Matthew Buckstein
Production Coordinators
Melissa Vukicevic
Devaro Bolton
Digital Campaign Coordinator
Alvan Au

ADVERTISING SALES
Sales Director
Joseph Galea
Director of Business Development
John MacPherson

FINANCE AND ADMINISTRATION
Chief Financial Officer
Philip Hartung
Senior Director of Operations
Krista Taylor
Accounting Manager
John Zhai
Accounting Assistant
Audrey Tang
Executive Administrative Assistant
Tim Broderick
Administrative Assistant
Helen McAuley

SENIOR VICE PRESIDENT, SALES
Peter Badeau
pbadeau@veterinarypracticenews.com

NATIONAL SALES MANAGER
William Rauch
wrauch@veterinarypracticenews.com

ACCOUNT MANAGER
Brenda Burns
bburns@veterinarypracticenews.com

Unless otherwise noted, images from ©Bigstock.com.

Brought to you by

Kenilworth MEDIA INC
A FORUM MEDIA GROUP COMPANY

ROYAL CANIN®
INCREDIBLE IN EVERY DETAIL™

Contents

Food for thought:

Dietary considerations in feline lower urinary tract diseases

By Kerry Rolph, BVM&S, CertVC, PhD, FANZCVS (feline chapter), DipECVIM-Ca, MRCVS

Cats frequently present with signs of feline lower urinary tract disease (FLUTD). It has been reported 4.6 percent of cats evaluated in private practices in the U.S. and seven to eight percent of cats seen at veterinary teaching hospitals present for lower urinary tract disorders (Forrester and Roudebush, 2007). Clinical signs frequently include: hematuria, stranguria, dysuria, periuria, pollakiuria, behavioral changes (such as aggression), and excessive grooming of the perineum and/or ventrum. Unfortunately, as the bladder can only respond to insult in a limited number of ways, the clinical signs are not predictive of the underlying disease process.

There are several diseases that can result in clinical signs of FLUTD. In cats older than 10 years of age, the most likely differentials are:

- urinary tract infection (UTI) (45 percent of cases);
- uroliths (10 percent of cases); and
- uroliths and UTI (16 percent of cases), with neoplasia, trauma, idiopathic disease, and urinary incontinence occurring in the remaining cases (Bartges, 2002).

Conversely, in cats younger than 10 years of age, the most common cause of lower urinary tract signs is idiopathic FLUTD (iFLUTD or feline interstitial cystitis [FIC]), which accounts for more than 50 percent of cases, with some further 20 percent of patients demonstrating urethral plugs. These are thought to arise from inflammation with crystal amalgamation. This has led many clinicians to believe this is a subset of iFLUTD, with these two

forms accounting for approximately 75 percent of cases (Caney, 2011). Between 15 and 21 percent of cases under 10 years of age will have urolithiasis, while only one to two percent of cats younger than 10 years old are found to have UTIs. Dietary management is important in the control of both urolithiasis and iFLUTD (Bartges, 2002).

Understanding uroliths

Formation of uroliths is not a disease per se, but can occur as a complication of another disorder. For example, 35 percent of cats presenting with calcium oxalate uroliths have been reported to be hypercalcemic. In other cases, the underlying etiopathogenesis may not be elucidated (Bartges and Kirk, 2006).

There are many minerals that can precipitate within the urinary tract to form crystals. The most common are struvite (magnesium ammonium phosphate hexahydrate) or calcium oxalate. However, crystals are found in many normal cats, and are not necessarily pathogenic. Factors influencing crystal formation include the amount of mineral saturated within the urine (*i.e.* whether or not supersaturation is present), urine pH, urine temperature, the presence or absence of various inhibitory factors such as citrate or pyrophosphate, and the occurrence of promoters of crystallization, including dead cells, cellular debris, protein, bacteria, or other crystals (Matsumoto and Funaba, 2008, Bartges and Callens, 2015). For urolith formation to occur, there must first be an initiation phase, which involves the formation of a crystal nidus (nucleation). Crystal growth depends on the ability of the nidus to remain within the urinary tract, the duration of supersaturation of the urine, and the crystal's physical ultrastructure. The actual rate of growth of the urolith depends on numerous factors, including mineral composition and risk factors such as infection (Bartges and Callens, 2015).

Struvite uroliths account for more than 50 percent of all feline uroliths (Bartges and Callens, 2015). These can occur as a consequence of infection of the urinary tract with a urease-producing bacterium (bacterial-associated uroliths) or can occur in sterile urine, where they are considered a dietary-induced urolith. Infection-induced struvite uroliths are reported to occur more commonly in cats younger than one year or older than 10 years of age (Bartges and Kirk, 2006). In cats, the majority of struvite uroliths are sterile. However, infection should always be ruled out as an underlying cause.

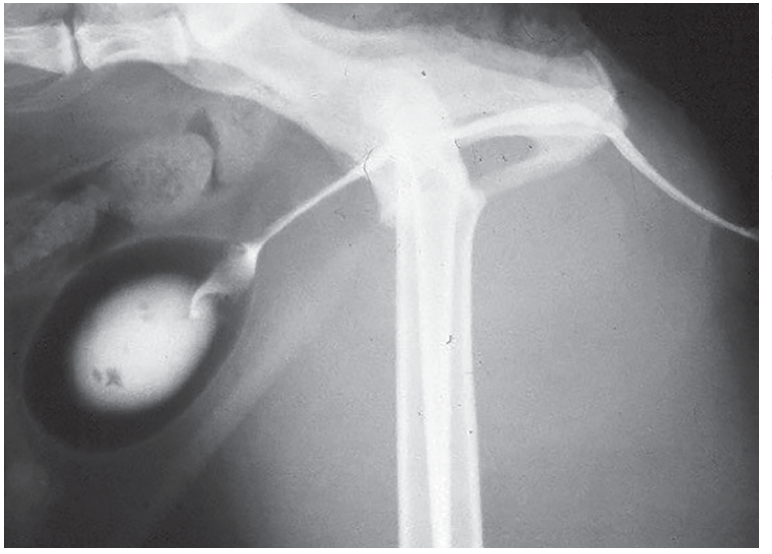


Photo courtesy Kerry Rolph

Stones in the urinary bladder on a double contrast radiograph.

Diet considerations

Sterile struvite uroliths occur most commonly in cats between one and 10 years of age. In at-risk cats (*i.e.* those with a lack of urolith inhibitors) fed a diet that leads to supersaturation of the urolith constituents, stone formation can occur. Decreasing urine concentration (and therefore retention time) has been shown to markedly lower the risk of urolith formation (Bartges and Callens, 2015). Experimentally, diets containing excessive amounts of

magnesium phosphate have led to the formation of sterile struvite uroliths in normal cats (Osborne et al. 1985). However, the influence of magnesium depends on the urinary pH, with alkaluria predisposing to struvite formation (Queau, 2019).

Struvite uroliths can be dissolved by feeding a diet that is acidifying, and one restricted in magnesium, phosphorus, and protein. In cats with sterile struvite uroliths, such a diet has been shown to lead to dissolution in approximately 36 days (range 14 to 141 days). However, in infection-induced struvite urolithiasis, this was increased to approximately 79 days (Bartges and Kirk, 2006). It is recommended that when infection-associated struvite urolithiasis is treated, the cat should remain on an appropriate antibiotic for the duration of dissolution and a further two weeks thereafter.

Diets manufactured for the dissolution of struvite uroliths should not be fed to the patient long-term, as they are not balanced and the acidification will predispose to calcium oxalate (or other) forms of urolithiasis. Therefore, after dissolution of sterile-struvite, the cat should be switched to a maintenance lower urinary tract diet that will do the following:

- dilute the urine, avoiding supersaturation;
- provide the nutritional requirements for the formation of urolith inhibitors; and
- maintain an appropriate pH to decrease the risk of either calcium oxalate or struvite uroliths.

Recently, one such diet has been shown to provide dissolution of struvite uroliths (albeit over approximately double to time frame of the dissolution diet) (Lulich et al. 2013). Infection-induced struvite uroliths do not need a maintenance diet, as once the infection is adequately treated, the risk for urolith formation is removed.

Calcium oxalate uroliths form when urine is supersaturated with calcium and oxalate. In addition, large molecular-weight proteins occurring in the urine, such as nephrocalcin, uropontin, and Tamm-Horsfall mucoprotein, affect the formation of calcium oxalate uroliths (Dijcker et al. 2011, Lulich et al. 2016). They account for approximately 35 percent of all feline uroliths submitted to one veterinary analysis laboratory (Minnesota Urolith Center, 2020). Hypercalcemia is present in 35 percent of cases with calcium oxalate uroliths; however, of cats presenting with idiopathic hypercalcemia, 35 percent have calcium oxalate uroliths (Bartges and Kirk, 2006).

Hypercalciuria can occur from excessive intestinal absorption of calcium, impaired renal reabsorption, or excessive skeletal mobilization. While hypercalciuria has not been well-defined in normocalcemic cats with calcium oxalate uroliths, it is thought to occur. Metabolic acidosis promotes hypercalciuria. As buffers are released from the bone, there is

concurrent release of calcium, which, in turn, increases urinary calcium excretion (Lekcharoensuk et al. 2000, Bartges et al. 2013).

It is recognized that consumption of diets supplemented with urinary acidifiers (*e.g.* ammonium chloride) is associated with increased urinary calcium excretion. Significant aciduria (urine pH <6.2) is thought to predispose to calcium oxalate formation, in part due to the associated academia and hypercalciuria. However, it is also recognized that acidic urine alters the function and concentration of crystal inhibitors (aciduria promotes hypocitraturia and leads to functional impairment of endogenous urolith inhibitors) (Bartges and Kirk, 2006). Substances such as citrate, magnesium, and pyrophosphate—which form soluble salts with calcium or oxalic acid—reduce the availability of these substances for precipitation (Bartges and Callens, 2015). Other inhibitors, such as Tamm-Horsfall glycoprotein and nephrocalcin, interfere with the ability of calcium and oxalic acid to combine and thereby minimize crystal formation, aggregation, and growth (Bartges and Kirk, 2006).

Oxalic acid is a metabolite of ascorbic acid (vitamin C) and several amino acids, including glycine and serine. If oxalic acid combines with potassium or sodium ions, it forms soluble salts. However, if it combines with calcium ions, the salt is insoluble. It is recognized an increase in dietary intake of oxalic acid (or vitamin B6 deficiency) can predispose to calcium oxalate formation (Dijcker et al. 2011).

Calcium oxalate uroliths cannot be dissolved by adjusting the patient's diet. Instead, they require interventional or surgical procedures if they are to be removed from the urinary tract. However, there are medical and nutritional interventions that are recommended to decrease the recurrence of these uroliths in at-risk cats (Lulich et al. 2016). The mainstay of treatment is to decrease urine concentration (and therefore supersaturation). In addition, diets have been formulated to promote high concentrations and activity of urolith inhibitors, reduce urine acidity, and decrease calcium and oxalate concentration within the urine (Lulich et al. 2016). Achieving a urine concentration below 1.030 not only leads to decreased saturation,

To reduce stress (which can contribute to idiopathic FLUTD), advise clients to provide at least one tray per cat, preferably with one extra tray in multi-cat households.

but results in an increased urine transit time and voiding frequency (Bartges and Kirk, 2006). This can be achieved by feeding wet food and adding water, or feeding a prescription diet designed to lower urine concentration and prevent urolith formation.

It has long been recognized that acidifying diets predispose to the formation of calcium oxalate uroliths. It is thought persistent aciduria leads to low-grade metabolic acidosis, and thereby increases bone metabolism and calciuria (Bartges et al. 2013). In addition, aciduria promotes hypocitraturia and functional impairment of endogenous urolith inhibitors. Therefore, feeding an acidifying diet or administering urinary acidifiers to a cat that is predisposed to calcium oxalate uroliths is contraindicated. To prevent recurrence of calcium oxalate urolithiasis, a urinary pH of 6.6 to 7.5 is advised (Lulich et al. 2016).

Aside from reducing urinary concentration and optimizing pH, decreasing urinary substrate can aid in lowering stone recurrence.

Therefore, it is advised the patient's diet contain a moderate level of calcium (marked restriction has been reported to increase urinary calcium levels in normal cats) and relatively low level of oxalate. Excessive amounts of vitamin D (which can increase calcium absorption and therefore cause calciuria) should be avoided. Since phosphate restriction can increase activation of vitamin D and in turn promote intestinal calcium absorption, it is recommended low phosphate diets are avoided (Bartges and Callens, 2015).

Urinary oxalate is derived from the following:

- endogenous metabolism of various amino acids (including glycine and serine);
- the metabolism of ascorbic acid (vitamin C); and
- dietary oxalic acid.

If there is inadequate vitamin B6 within the diet, oxalic acid production and urinary excretion is increased. Kittens fed a B6-deficient diet have been shown to develop calcium oxalate urolithiasis (Blanchard et al. 1991). Therefore, cats with a history of calcium oxalate urolithiasis should receive a diet low in oxalic acid and with adequate B6, while excess intake of vitamin C should be avoided. For this reason, cranberry concentrate should be avoided, as it not only provides mild acidification, but also contains high levels of oxalate and vitamin C (Bartges and Kirk, 2006).

In refractory cases of calcium oxalate urolithiasis, potassium citrate may be included in the diet or as an additional medication. As stated previously, citric acid can combine with calcium to form a soluble complex, thereby reducing the amount of calcium available for urolith formation. In addition, citric acid inhibits nucleation of calcium and oxalate crystals (Bartges, 2002). In a similar manner, urinary magnesium complexes with oxalic acid, decreasing the amount available to form uroliths. Cats receiving a diet deplete in magnesium have been shown to be at increased risk of calcium oxalate urolithiasis. However, excess magnesium should be avoided, as it can predispose to struvite formation (Osborne et al. 1985).

Idiopathic feline lower urinary tract disease

In young to middle-aged cats presenting with signs of FLUTD, idiopathic disease is the most likely differential. Studies have highlighted several predisposing factors for this condition. The cats are:

- male, neutered, and overweight;
- use a litter tray;
- rarely go outside;
- have limited exercise; and
- typically live in a multi-cat household (Gunn-Moore, 2003).

In addition, black and white cats, as well as Persians, demonstrate an increased incidence of disease (Gunn-Moore, 2003). Bladder signs are typically self-limiting, and unless obstruction occurs, usually resolve without treatment in three to five days. However, our understanding of this condition has evolved in recent years. Current belief is that this is in fact a systemic condition, with clinical signs attributed to the

It's been reported that 4.6 percent of cats evaluated in private practices in the U.S. and seven to eight percent of cats seen at veterinary teaching hospitals present for lower urinary tract disorders.

urinary bladder and abnormalities identified within the brain, spinal cord, and adrenal glands in addition to the bladder wall (Buffington, 2011). Cats with idiopathic cystitis demonstrate alterations within the glycosaminoglycan (GAG) layer. Although a generalized decrease in the GAG layer and a reduction in the GAG GP-51 have both been reported in cats, studies attempting to replenish the former have failed to demonstrate a benefit above that seen with placebo medications (Press et al. 1995, Buffington et al. 1996, Gunn-Moore and Shenoy, 2004, Pereira et al. 2004). In addition, the urothelium, which normally forms a tight barrier to ion and solute flux, is more permeable in cats with idiopathic cystitis; on electron microscopy, a denuded urothelium has been identified (Lavelle et al. 2000).

Within the submucosa, signs consistent with neurogenic inflammation (vasodilation and vascular leakage in the absence of significant mononuclear or polymorphonuclear infiltration) have been reported, along with increased mast cell numbers in some cases (Buffington, 2011). However, changes are not limited to the bladder wall, with multiple neuroendocrine abnormalities being present. For example, the mechanoreceptor bladder afferent neurons appear to be more sensitive to stimuli in affected cats. In addition, there is an increase in the expression of substance P (a sensory neurotransmitter) receptors (Gunn-Moore, 2003), enlargement of the cell bodies within the dorsal root ganglion, and abnormal neuropeptide profiles within the dorsal root ganglion. This is not restricted to the cells from bladder-identified neurons, but affects cells throughout the lumbosacral spinal cord (Buffington, 2011).

The role stress plays

It is well documented in both laboratory studies and client-owned cats that exacerbations of lower urinary tract signs occur with external environmental stressors. It is known that cats with idiopathic cystitis have increased levels of tyrosine hydroxylase (the rate-limiting enzyme involved in catecholamine synthesis) within the locus coeruleus and paraventricular nucleus of the hypothalamus (Buffington and Pacak, 2001). In addition, it has been shown there is greater activity in the locus coeruleus, an area of the brain that not only deals with vigilance and arousal, but in which the highest number of noradrenergic neurons are found. It is also an important source of noradrenaline within the central nervous system (CNS). In addition, chronic external stress is known to escalate the activity of tyrosine hydroxylase with accompanying increases in autonomic outflow (Buffington, 2011). Cumulatively, these alterations lead to an altered response to stress.

Stress can be a factor in multi-cat households, contributing to idiopathic FLUTD.

Normal cats respond to stress with activation of the hypothalamic-pituitary-adrenal (HPA) axis. This is seen as increased activity in the locus coeruleus, higher plasma catecholamine concentrations, enhanced adrenal sensitivity to adrenocorticotropic hormone (ACTH), greater secretion of glucocorticoids from the adrenal cortex, and increased urine cortisol concentrations. The role of glucocorticoids and other alpha-2 adrenoceptor agonists is complex. However, one of their

essential functions is to provide negative feedback to control the stress response, which they do by inhibiting further transmission of noxious signals to the brain.

In contrast, cats with idiopathic cystitis respond to stress in a different manner. They are likely to demonstrate displacement activity such as increased eating, drinking, grooming, and urinating. While they do show markedly increased activity in their locus coeruleus and significantly increased sympathetic activity compared to normal cats, this does not appear to be restrained by adrenocorticotrophic output; an inappropriate activation of the adrenal cortex and decreased sensitivity to ACTH are seen in cats with idiopathic cystitis (Gunn-Moore, 2003). This uncoupling of the hypothalamic-pituitary-adrenal axis is also seen in some chronic pain syndromes in humans and is believed to result from desensitization or down-regulation of the alpha-2 adrenoceptor agonist receptors, secondary to chronic stimulation. While a recent study has shown cats with idiopathic cystitis have multiple abnormalities in their alpha-2 adrenoceptor-mediated signal transduction pathway, it is still unclear whether this represents adaptation to living with chronic stress or indicates these cats have an innate defect in their ability to cope with stress (Buffington, 2011).

In addition to the changes within the bladder and neuroendocrine system, it has been documented that cats with idiopathic cystitis are more likely to demonstrate a range of other abnormalities that together have been termed "sickness behaviors." Studies of confined animals have shown sickness behaviors can occur with activation of the stress response system and result in a variety of signs such as anorexia, sickness, inappetence, diarrhea, enhanced pain behavior, and general ill-thrift (Buffington, 2011). Putting these findings together, it becomes evident that while cats with idiopathic cystitis appear to have disease of the urinary bladder, they are, in fact, suffering from a far more complex syndrome with wide-reaching effects. This is important to keep in mind when treatment decisions are being made.

Figure 1

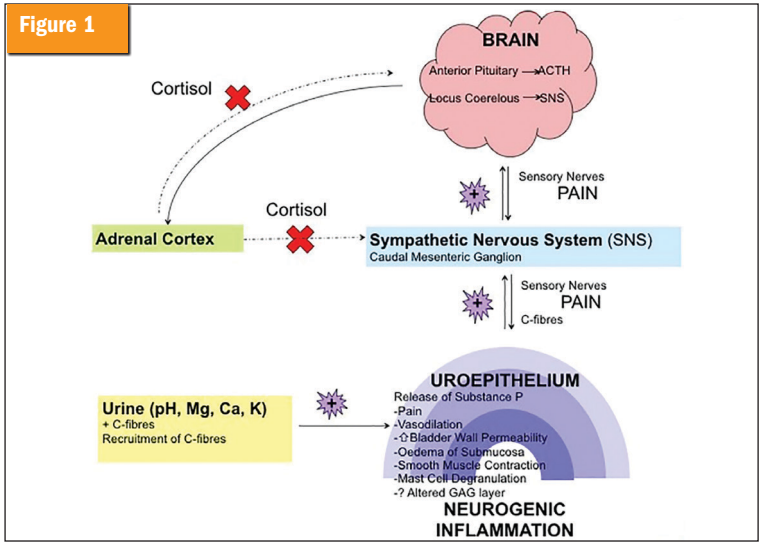


Photo courtesy Kerry Rolph

Current hypothesis for neurogenic inflammation in FIC. (Adapted from: Buffington, Chew and DiBartola (1996)).

Approach to a cat with hematuria/dysuria/stranguria

When presented with a cat with clinical signs consistent with lower urinary tract disease, it is important to gain an accurate history. Is the cat at increased risk of UTI? This condition accounts for about two percent of cases of cystitis in cats under 10 years of age, and is rare in concentrated urine (Gunn-Moore, 2003). To rule out UTI, a urine sample should be obtained, and urine specific gravity (USG) and culture of the urine performed.

The second big rule out is whether uroliths are suspected. Consider first the cat's diet. Could the food predispose the patient to urolith formation? Does the cat have a history of uroliths or is it a breed known to be predisposed to urolith formation such as the ragdoll or British short-haired breeds? (Lekcharoensuk et al. 2000). If a cat is thought to be at risk of calcium oxalate uroliths, blood calcium (ideally ionized calcium) should be obtained to rule out systemic

hypercalcemia as the cause of urinary supersaturation and secondary stone formation. Where possible, diagnostic imaging (ideally a double contrast pneumocystogram) should also be performed to rule in/out urolith formation. If uroliths are identified, examining the urine for crystals and assessing the pH might be suggestive of the type of urolith. This, however, does not definitely prove the type of stone. If a suspected struvite urolith doesn't respond appropriately to medical management, surgery and stone analysis may be indicated. Any cat with uroliths should have a urinary culture performed to rule out primary or secondary infection.

If neither UTI nor uroliths is suspected and the cat is younger than 10 years of age (making neoplasia less likely), treatment for idiopathic cystitis can be instigated. Cases should be reviewed regularly—if the response is not optimal, further investigations may be needed.

As discussed, idiopathic FLUTD is a multisystem disease, requiring a multimodal approach to treatment. Dealing with bladder signs alone will not demonstrate an overall benefit to the cat, who will continue to have abnormal stress response and may demonstrate sickness behaviors (Buffington, 2011). Provided the cat is not obstructed and renal function is adequate (as assessed by the USG at a minimum), environmental enrichment to decrease stress, dietary alterations, and pharmacological intervention can be considered. The owner should be aware this is a disease of unknown cause, with no known cure. Therefore, the goal of therapy is to reduce the severity and recurrence rate of subsequent episodes.

Considering the evidence stress plays in this syndrome's etiology, stress reduction is thought to be of great importance. Measures that should be taken include:

- assessment of the cat's environment, ensuring the individual has minimal interactions with more playful cats in the household;
- making sure the cat isn't exposed to loud or sudden noises and has "safe passage" to a litter tray (which should be of a design and incorporate a substrate the patient finds preferable);

Cats who are male, neutered, and overweight; use a litter tray; rarely go outside; and have limited exercise are predisposed to feline lower urinary tract disease.

- situating trays close to the cat's "safety zone" within the home, away from high-traffic areas with at least one tray per cat, preferably with one extra tray in multi-cat households; and
- identifying the cat's stressors and providing ample "safe zones" away from these to encourage the cat to move around more, enhancing his or her quality of life in general.

This final point can be a lengthy process and might involve asking the owner to draw a map of the cat's territory and core zones, identifying where interactions and stressors might be located. In addition, synthetic pheromones or supplements aimed at stress reduction (*i.e.* the milk protein, hydrolysate alpha-casozepine) may help decrease stress in some individuals, and therefore decrease clinical signs (Gunn-Moore and Cameron, 2004, Beata et al. 2007).

Lowering the cat's urine specific gravity has demonstrated the greatest benefit. Cats with a USG less than 1.030 have a significantly reduced recurrence of signs compared to those with a USG greater than 1.030 (Buffington, 2011). Therefore, implementing changes in diet and water consumption can greatly decrease recurrence. This can be achieved by providing alternative sources of water around the home (water fountains, glasses, rain water), flavoring water with tuna juice, etc., or feeding a wet diet or a diet designed to promote diuresis (Gunn-Moore, 2003). Recently, commercially available prescription diets have been introduced that are designed to dilute urine. Studies have demonstrated a significant decrease in the recurrence of idiopathic FLUTD with such diets, even when dried formulations are fed. In addition, some manufacturers have supplemented these diets with glycosaminoglycans (GAGs) and substances aimed at reducing stress such as alpha-casozepine and tryptophan (as a serotonin precursor) (Naarden and Corbee, 2020). These formulations, which decrease urolith formation by avoiding supersaturation of the urine with the composite minerals, dissolve struvite uroliths (although more slowly than the diets designed specifically for this) and decrease the incidence of iFLUTD. As such, they are appropriate for long-term management

of many feline lower urinary tract diseases (Lulich et al. 2013, Naarden and Corbee, 2020). ●

Kerry Rolph, BVM&S, CertVC, PhD, FANZCVS (feline chapter), DipECVIM-Ca, MRCVS, is an associate professor of small animal internal medicine at Ross University School of Veterinary Medicine (RUSVM). She graduated from Edinburgh University and worked in small animal practice for two years before returning to Edinburgh to study for her PhD. Dr. Rolph gained both her certificate in veterinary cardiology and PhD in 2004. In 2010, she passed the Feline Medicine Australian College of Veterinary Scientists Fellowship examinations. Four years later, Rolph gained her European diploma in companion animal medicine and became a European specialist in companion animal medicine. She then worked at a private referral hospital in Bristol, England, for three years before joining RUSVM in January 2019. Rolph can be contacted via email at KRolph@rossvet.edu.kn.

View references for this article at veterinarypracticenews.com/FLUTD-august-2020.

Implementing changes in diet and water consumption can greatly decrease recurrence of idiopathic FLUTD. This can be achieved by providing alternative sources of water around the home, flavoring water with tuna juice, etc., or feeding a wet diet or a diet designed to promote diuresis.

ROYAL CANIN®

A CUTTING EDGE INNOVATION FOR LOWER URINARY TRACT DISEASE MANAGEMENT IN AGING CATS AND DOGS

Nutrition can play a key role in urinary patients' recovery and ongoing health at any age. That's why we developed a cutting edge innovation in urinary health and expanded our line to target specific urinary conditions in aging pets.

URINARY TRACT HEALTH
Effective struvite stone dissolution & specifically formulated for up to 80% of all urinary stones.*

COGNITION AND VITALITY AGING SUPPORT
Support pets' vitality, cognition and kidney health with an exclusive blend of nutrients & antioxidants.

HIGHLY PALATABLE PRODUCTS
Help support the poor appetites of aging cats and dogs.

URINARY SECURITY
Relative supersaturation (RSS) methodology predicts the crystallization potential of urine. RSS is used to develop diets that lower the concentration of ions contributing to struvite and calcium oxalate urolithiasis.

Contact your Royal Canin brand representative for details and ordering information.

*Houston DM, et al. Can Vet J 2016; 57: 196–201. *Houston DM, et al. Can Vet J 2017; 58: 45–50.

URINARY

HYDRATION
INCREASE THE WATER INTAKE TO HELP DILUTE URINE

CAT
9-23 ml per lb[5]
Daily water requirement

DOG
23-27 ml per lb[5]
Daily water requirement

WET OR SPECIFIC DRY FORMULAS COULD INCREASE WATER INTAKE

ROYAL CANIN® DIETS
help increase water intake to facilitate RSS performance in mixed feeding

Other features include:

- High quality proteins
- Controlled and balanced mineral content
- Specific nutrients such as L-tryptophan or alpha-casozepine to manage FIC

ROYAL CANIN® RSS PERFORMANCE

LABILE SUPERSATURATION
Crystal formation

METASTABLE SUPERSATURATION
Crystal solubility

UNDERSATURATION
No crystal formation and dissolution of pure struvite uroliths

[5]National Research Council, *Nutrient requirements of dogs and cats*, 2006. Food moisture content: Wet food = 85%, Dry food = 9%

Stoner news:
Struvite diets for cats and dogs

By Kim Campbell Thornton

An improved understanding of the role of pH, magnesium, and phosphorus; greater knowledge of risk factors; and more dietary options have changed how struvite stones are treated in cats and dogs. While struvite uroliths may in some cases require surgical intervention, the recommended standard of care by the American College of Veterinary Internal Medicine (ACVIM) is medical dissolution with a therapeutic diet formulated to alter urine acidity and encourage water consumption.

Dietary dissolution of struvite stones is both effective and inexpensive. Therapeutic diets limit calculogenic compounds (*e.g.* phosphorus and magnesium) and acidify urine. That makes the urine a less welcoming environment for stone formation and dissolves stones that are present.

Concerns medical dissolution places pets at risk of urethral obstruction are not borne out by the literature, according to the ACVIM consensus statement, published in the *Journal of Veterinary Internal Medicine (JVIM)* in 2016.

Dietary management itself has changed as well. The shift from struvite-only dissolution or prevention diets to combination struvite dissolution/prevention and calcium oxalate prevention diets is the biggest change in management of these uroliths, says Cailin Heinze, VMD, Dipl. ACVN, assistant professor of nutrition at Cummings School of Veterinary Medicine at Tufts University.

Causes differ

Struvite uroliths occur in both dogs and cats, but have different causes. In dogs, struvite stones—the most common type seen—develop almost

exclusively as a result of urinary tract infections (UTIs) caused by urease-producing bacteria. Female dogs are at greater risk, as they are more likely to develop UTIs. Breeds at higher risk include bichons frise, miniature schnauzers, Shih Tzu, and pekingese.

Cats, on the other hand, produce struvite metabolically, in the absence of a urinary tract infection.

While a therapeutic diet is effective for cats and dogs, length and type of treatment varies. In dogs, use of a therapeutic diet is typically short term and accompanied by identification of and treatment for UTI. Depending on the size and number of stones, they may dissolve in as little as two to three weeks or as long as two to three months.

A diet formulated to treat struvite urolithiasis won't prevent recurrence in dogs, but according to ACVIM consensus recommendations, it may delay or minimize urolith burden if a UTI goes unrecognized. Once stones are dissolved, the goal is to prevent or treat future infections.

Cats are different

Cats may have predisposing factors to struvite stones, such as castration, obesity, and a sedentary lifestyle. Struvite urolithiasis is more common in females and in castrated males, says Bruce Kornreich, DVM, Dipl. ACVIM. The highest incidence appears to be in cats two to seven years old.

Dr. Kornreich notes owners of cats who develop struvite stones may need to control their pets' weight through diet and exercise, in addition to feeding a struvite-prevention diet.

When cats develop struvite, risk of recurrence is reasonably high, Dr. Heinze says. "You presume that whatever led to it in the first place has not been resolved."

For that reason, she says, cats with a history of struvite stones should stay on a therapeutic diet long term. (The exception to dietary dissolution is cats with obstructive upper urinary tract uroliths, which should be removed through minimally invasive procedures.) As with dogs, struvite dissolution diets are inappropriate for kittens or pregnant or lactating female cats.

Cats with a history of struvite stones should stay on a therapeutic diet long-term.

Once cats are eating the dissolution diet, re-radiograph them every two to four weeks, says Tony Buffington, DVM, PhD, Dipl. ACVN. Sterile struvite urocystoliths typically dissolve over a period of two to five weeks. Dr. Buffington recommends having owners continue feeding the diet for at least 30 days after uroliths are no longer visible radiographically.

"The rate at which uroliths dissolve is proportional to the surface area of the urolith exposed to the undersaturated urine," he says. "Small, sterile struvite uroliths may dissolve in as little as one to two weeks. Struvite dissolution diets do not dissolve nonstruvite uroliths and are less effective if a persistent UTI is present or the cat is fed anything in addition to the dissolution diet."

Canned versus dry

Therapeutic diets are available in canned and dry varieties. Feeding canned food improves water intake, making urine less concentrated

and ensuring saturation by calculogenic compounds is lower. Choice is based on owner preference, pet preference, normal pet water intake, and desired goal.

For stone prevention, canned food is desirable because of its high moisture content.

"When you're trying to dissolve or prevent any type of urinary stone, having very diluted urine is critical," Heinze says. "Typically, if your goal is dissolution and you can afford to feed it to a larger dog or if a cat will eat it, canned therapeutic food is always going to be ideal. But if you need to dissolve struvite stones or you need to prevent them in a cat, you're probably better with a dry struvite-prevention and dissolution diet than with a canned, nontherapeutic diet."

Pets who normally drink plenty of water can do well on a dry struvite-prevention diet, though, or one moistened with water or broth. In Buffington's experience, most cats prefer canned food to dry food with water added to it. Most dogs who eat dry food tolerate the addition of one cup of water to every cup of dry food.

Transitioning foods

Dissolution diets work best when no other foods are permitted. Switch the animal from the normal diet to a dissolution diet over a period of about a week. Cats tend to be more neophobic regarding therapeutic diets than dogs, but of course they are all individuals. Some take to the new diet with no reluctance. With dogs or cats, it's best to start a new food when the pet is feeling good again, rather than immediately after surgery or illness.

Getting pets to eat struvite diets is less of a problem than in the past. With four canned and dry options for dogs and a similar number for cats, it's easier to find one a pet will like, Heinze says.

"I would say the biggest issue tends to be if they have other health problems," she adds.

For instance, some stone-prevention diets are high in sodium. That encourages pets to drink more water and dilute the urine, but it makes these diets inappropriate for animals with congestive heart failure, high blood pressure, chronic kidney disease, or other conditions sensitive to sodium. In those cases, check labels carefully to make sure you are recommending a lower sodium option.

Cats produce struvite metabolically, in the absence of a urinary tract infection.

To move animals onto the new food, Buffington recommends offering half the daily ration of the familiar food and half as the new food in separate containers at mealtime, if owners feed once a day. Over several days, owners can gradually reduce the amount of the familiar

food and increase the amount of the struvite diet. Flavoring food with chicken broth can help to draw the pet's interest.

If animals refuse to eat a therapeutic diet, be familiar with some of the supermarket brands that may offer similar if incomplete benefits.

"There have been cases I'm aware of where cats won't eat the [therapeutic] diet, but might eat these sorts of urinary tract diets from a supermarket," Kornreich says. "If you can't decrease magnesium content tremendously, it makes sense to lower it as much as you can. Same with pH effect and same with phosphorus concentration."

Cautions and exceptions

Heinze says leaving dogs on a struvite dissolution or prevention diet after stones have dissolved is the biggest management mistake she sees. It's not unusual for her to talk to clients whose dogs have been on struvite prevention diets unnecessarily for long periods. Drawbacks to keeping dogs on the foods needlessly are added cost and inconvenience for owners. Another is that not all struvite dissolution diets contain adequate nutrients for longer term feeding. None of the struvite dissolution and prevention diets are appropriate for young animals or pregnant or lactating female dogs.

"The struvite-calcium oxalate combination diets are designed to meet maintenance nutrient requirements, but that doesn't mean they're ideal if you didn't need one," Heinze says.

Due to their extreme reductions in nutrients (*e.g.* protein, magnesium, and phosphorus), diets designed for struvite prevention are for short-term use only. If clients are feeding one of these foods, follow up closely to make sure they don't keep the pet on it.

"I had owners come in that were feeding one of the strict struvite-only dissolution diets for a year," Heinze says. "The diet is very, very low in protein, and that dog actually had low blood proteins, likely because of dietary deficiency."

The exception to short-term use of struvite-prevention diets in dogs is when a dog may have abnormal perineal conformation or is otherwise predisposed to urinary tract infections, Heinze says. For dogs with recurring infections from urease-producing bacteria, feeding a nutritionally balanced therapeutic diet over the long term may provide some reduction of stone risk.

It is recommended not to leave dogs on a struvite dissolution or prevention diet after stones have dissolved.

Owners often want to know if other pets in the household can eat the same food. The answer is maybe.

"You're probably fine to put another pet in the household that doesn't have a history of stones on one of those struvite-oxalate combo diets, as long as they don't have any other health issues," Heinze says. ●

ROYAL CANIN®
HEMATURIA DETECTION
technology by
blücare®

MAKE PROACTIVE WELLNESS PART OF YOUR PRACTICE

with Our Breakthrough At-Home Hematuria Detection

Royal Canin Hematuria Detection, Technology by Blücare is composed of litter granules for early blood detection in feline urine. We developed this to help support your practice, ease the monitoring, and ease the follow-up for early detection of recurrence in support of better cat health.

ROYAL CANIN® HEMATURIA DETECTION BY BLÜCARE

CAT

Allows to perform blood detection in a **non-invasive manner**

No change needed in litter or environment

Improves early detection of urinary conditions

OWNER

Provides reassurance by allowing the cat owner to monitor their cat's urinary health at home

Earlier detection of urinary issues

VET

Increase the chances to see patients at an **early stage of disease**

A way to **provide better service** to your clients & strengthen the veterinary-client-patient relationship

Process and usage **is very easy to explain** to the client

Helps drive **compliance** between the cat owner and your recommendation

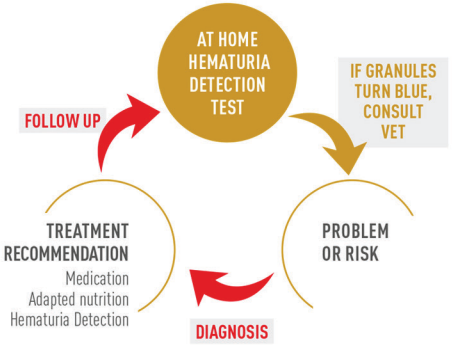
WHAT IT IS

When hemoglobin is detected in feline urine, a chromogenic enzyme reaction occurs, turning the white litter granules BLUE. This color change helps cat owners determine that a veterinary consult is needed.*

*Test results may vary based on conditions of use and other factors such as a cat's diet and medication. Each test has its limitations, false positives, and false negatives. Accuracy of results is not guaranteed.

WHEN TO USE IT

HEMATURIA DETECTION is a tool to be used in proactive urinary monitoring.



HOW IT WORKS

3 EASY STEPS

1. 
Spread the granules over the litter and wait for your cat to urinate.

2. 
Inspect the litter box after your cat urinates.


If granules are WHITE or YELLOW, the test is negative.


If they turned blue, the test is positive, as it shows the presence of blood in the cat's urine.

3. 
If granules turn BLUE, contact your veterinarian to confirm results.

Bacterial infections:

Resistance isn't necessarily futile

By Don Jergler

Primary health-care providers in veterinary and human medicine face the same problem when it comes to client expectations.

"Various studies suggest human patients and their primary health providers may not be on the same antibiotic page," says Dan Carey, DVM, a veterinarian with Bayer Animal Health. "Primary care providers tend to think most patients expect something to treat their ailment, while patients tend to be the converse: 'If I don't need it, just help me feel better somehow.'"

His advice? Clinicians should ask clients what their expectations are; then as educators, take the opportunity to explain the options.

"We do not have to reflexively reach for a seemingly innocuous antibiotic just so the client has something to take," Dr. Carey says. "But the client needs to know what we have chosen, why it was selected, and how it is properly used to get the expected response."

Heather Loenser, senior veterinary officer for the American Animal Hospital Association (AAHA), agrees. She wants veterinarians to understand the seriousness of antimicrobial resistance (AR).

"In an effort to control AR, antimicrobial use should be confined to appropriate clinical indications," says Dr. Loenser, adding veterinarians

should establish a definitive diagnosis whenever possible and avoid empirical use.

"Practitioners should strive to rule out viral infections, parasitism, mycotoxicosis, nutritional imbalances, and other ailments that will not respond to antimicrobial therapies," she says.

Many times, antimicrobial therapy just isn't the answer. It's not indicated in most viral upper respiratory infections (*e.g.* feline herpesvirus or calicivirus and canine influenza), which are not suspected to be complicated by secondary bacterial infection, according to Loenser.

For example, instances where antimicrobials are not indicated include cases of pancreatitis in dogs and cats, which do not have a bacterial component, and most cases of feline lower urinary tract disease also do not involve bacterial infection.

"Many pet caregivers, especially parents of young children, understand how physicians are reluctant to treat fevers, ear infections, and colds with antibiotics, for the same reasons—namely AR," Loenser says. "Reminding [them] of the consequences of creating bacteria in their pet, their home, and local environment that are difficult to treat can be compelling."

She also recommends educating the entire staff "from front to back" to deliver a unified message to clients who come in demanding antibiotics.

Far from a new issue, AR has been looming since the first antibiotics were developed, Carey says.

"Sir Alexander Fleming predicted the clinical implications when he discovered penicillin in the 1920s," he added. "Bacteria have always had enough susceptibility variation that some may survive and propagate a resistant subpopulation when faced with naturally occurring antibacterial compounds or human-made drugs. It has become increasingly important clinically, as continued selection pressure has allowed unaffected phenotypes to survive."

While certain bacterial species have always been unaffected by some antibacterial drugs, this type of resistance is not the real concern. The problem lies in the species that were once susceptible to specific antibiotics, but have lost that vulnerability, according to Carey.

"The development of new classical antibacterial molecules for veterinary medicine has virtually stopped," he says. "We have what we are going to have until some breakthroughs occur. This situation makes the long-existing reality of resistance a very topical problem for clinicians, clients, and patients."

Veterinarians should consider not culturing the urine of animals who don't have signs of lower urinary tract disease and not treating animals with subclinical bacteriuria unless a systemic bacterial infection is suspected.

Breaking old habits, considering alternatives

Jane Sykes, PhD, BVS, an academic administrator and professor of medicine and epidemiology at the University of California, Davis, offers a list of questions companion practitioners should ask themselves before reaching for antibiotics:

- Is this a condition that might not require antibiotics for successful treatment?
- If a bacterial infection is likely, what is the underlying cause, and how can I address it so repeated bacterial infections do not occur?
- If a bacterial infection is likely, what is the most appropriate empiric antibiotic, given the site of the infection, and what is the shortest duration of treatment that might cure the infection?
- Is there an opportunity to do culture and susceptibility testing before starting empiric treatment, in case this is a resistant infection, and what's the best sample for testing?

"Companion animal practitioners can work toward the need to control AR by considering alternatives to antibiotics for treatment," Dr. Sykes says.

But the axiom that old habits are hard to break rings even louder when met with the steadfast habits of both practitioners and clients.

Carey recalls advice an elder physician offered to a friend about her respiratory problem. The physician told her the issue would improve in a week if it was left to run its course or in seven days if an antibiotic was prescribed.

"This very simple statement sums up the challenge we face as clinicians: knowing the difference between a responsive bacterial infection and a primary, nonbacterial disease," he says.

Knowing is only a first step; the entire process isn't so easily followed in reality.

"Clients often balk at the cost of diagnostics," Carey says. "When allowed, diagnostics are not always, well, diagnostic. And regardless of the diagnostic outcome, clients often want something to give their pet."

There is no shortage of cases when other nonantibiotic drugs might be as effective at helping patients feel better while letting immunologic defense systems do their work. Symptomatic support with bronchodilators, analgesics, antipruritics, decongestants, pre/probiotics, and nutritional support, also can provide benefit without the risk of selecting for resistance, according to Carey.

"We must always remember that our patients have thousands of bacteria living in them all the time," he says. "Some are potential pathogens held in check by the system. Using any antibacterial drug has the potential to select for a resistance strain of the innocent bystander that can later become a full-blown pathogen with a nasty resistance pattern on the antibiogram."

Carey is among many experts who refer to the International Society for Companion Animal Infectious Diseases (ISCAID) guidelines for antibacterial stewardship, which are based on scientific information. These guidelines can be useful in helping decide when and when not to use antibacterial drugs.

"We are responsible for the proper drug choice," Carey says. "The client is responsible for compliant use. Compliance is dependent upon the client understanding the need for the drug and the importance of completing the prescribed protocol. Inadequate antibacterial dosing is a recipe for bacterial resistance."

Education is fundamental to compliance, but so is ease of use. A drug that can be administered in-clinic stands a much better chance of compliant use, while the dosage form—liquids are typically easier in cats than pills and easier for owners to administer—needs to match both the patient and the client, according to Carey.

Specific considerations

If practitioners do begin antibiotics, Sykes recommends starting with a short course—three to five days for urinary tract infections (UTIs), seven to 10 days for respiratory, and one to two weeks for skin. After 24 to 48 hours, consider an "antibiotic time-out" to figure out whether there is a response to treatment, if antibiotics can be stopped, or if there are other treatments that might be more effective.

She also recommends knowing the difference between subclinical bacteriuria and a urinary tract infection, and how they should be treated.

"Subclinical bacteriuria is bacteria in the urine without the presence of signs of lower urinary tract disease," Sykes says. "A diagnosis of bacterial UTI requires the presence of dysuria, hematuria, or stranguria. Subclinical bacteriuria is common, especially in older animals, and often does not require or respond well to antibiotic treatment."

Veterinarians should consider not culturing the urine of animals who don't have signs of lower urinary tract disease and not treating animals with subclinical bacteriuria unless a systemic bacterial infection is suspected, she added.

Guidelines on judicious use of antimicrobials

Basic Guidelines of Judicious Therapeutic Use of Antimicrobials from the American Association of Feline Practitioners (AAFP) and the American Animal Hospital Association (AAHA) emphasizes such preventive strategies as appropriate husbandry and hygiene, routine health monitoring, and vaccinations. In addition, the resource recommends therapeutic antimicrobial use should be confined to appropriate clinical indications:

- Establish a definitive diagnosis whenever possible; avoid empirical use
- Rule out viral infections, parasitism, mycotoxicosis, nutritional imbalances, and other ailments that will not respond to antimicrobial therapies
- Antimicrobial therapy is not indicated in most viral upper respiratory infections not suspected to be complicated by secondary bacterial infection
- Most cases of pancreatitis in dogs and cats have no bacterial component
- Most cases of feline lower urinary tract disease do not involve bacterial infection; in such cases, antimicrobials are not indicated

''Therapeutic alternatives should be considered prior to antimicrobial therapy,'' the guidelines state. ''This includes supportive care, such as correction of fluid and electrolyte abnormalities, maintaining acid-base balance, and ensuring adequate nutrition. Surgical intervention may be necessary in some cases. The use of antimicrobials to prevent infection can only be justified in cases where bacterial infection is likely to occur.''

Find the full guidelines at bit.ly/2P4f4uX.

Sykes advises educating pet owners through discussion of problems with antibiotic-resistant bacteria in pets, how treatment only selects for resistant bacteria when the underlying cause is not addressed, and how some infections now are virtually untreatable or require intravenous antibiotics.

Practitioners can instruct clients as follows:

- The overwhelming majority of cats with lower urinary tract signs do not have bacterial infections; time or analgesics and a workup for stones is a better strategy than treatment with antibiotics
- Almost all adult dogs with chronic nasal discharge (greater than 10 days) do not have a problem that can be treated successfully with antibiotics. An early diagnostic workup to look for foreign bodies, fungal infection (nasal aspergillosis), and nasal tumors could dramatically improve the long-term outcome compared with trying different courses of antibiotics for a secondary bacterial infection
- Most dogs with kennel cough and cats with acute (less than 10 days) upper respiratory tract disease do not need antibiotics
- Antibiotics do not change the outcome in cats and dogs with uncomplicated diarrhea and should be avoided in this situation AR is a big problem that demands attention, says Sykes, adding reports of resistant bacterial infections in her hospital have increased progressively over the last five to 10 years.

"We are increasingly facing situations where we only have parenteral treatment options with drugs that are potentially toxic or expensive, such as aminoglycosides or carbapenems (meropenem)," she says. "Companion animal practitioners must be proactive and responsible in their approach to antibiotic use, or we will be faced with watching individual animals suffer or die in the face of antibiotic-resistant bacterial infections despite our best efforts in that individual situation." ●

Five principles critical to antimicrobial stewardship

American Veterinary Medical Association's (AVMA's) Antimicrobial Stewardship Definition and Core Principles document outlines five principles to develop antimicrobial stewardship plans in any veterinary practice.

1) Commit to stewardship
   - Engage all practice members and relevant stakeholders in the stewardship effort
   - Develop plans that incorporate accountability for disease prevention and also optimize the prescribing, administration, and oversight of antimicrobial drugs
   - Identify high-priority conditions commonly treated with antimicrobial drugs on which to focus stewardship efforts
   - Commit to systematically assessing the outcomes of antimicrobial drug therapy
   - Identify someone to lead the stewardship plan
2) Advocate for a system of care to prevent common diseases
   - Identify barriers to improving disease prevention
   - Work with clients to adopt preventive and management strategies
   - Consider alternatives
3) Select and use antimicrobial drugs judiciously
   - Identify barriers to appropriate antimicrobial prescribing and usage
   - Use an evidence-based approach for making a diagnosis and determining whether antimicrobials are indicated
   - Make an informed selection of an appropriate antimicrobial drug and regimen
   - Refer to relevant veterinary medical guidelines for judicious therapeutic use
   - Assess outcomes of antimicrobial use
4) Evaluate antimicrobial drug use practices
   - Encourage development of a program for the evaluation of antimicrobial drug prescribing
   - Ensure feedback is provided to veterinarians
   - Support analyzing and sharing of antimicrobial drug use data
   - Engage clients to identify barriers to implementation of stewardship programs
   - Educate and build expertise
   - Encourage the development of expertise in antimicrobial stewardship
   - Stay current on strategies for disease prevention, and use of antimicrobial alternatives
   - Implement existing clinical guidelines for antimicrobial use
   - Provide client education on antimicrobial stewardship

Find the full guidelines at bit.ly/2NUjDv6.