Bacterial urinary tract infection (UTI) occurs in approximately 14% of dogs in their lifetime, with a variable age of onset. Animals with a UTI can present with stranguria, pollakiuria, dysuria and urinary incontinence, although some animals may have no clinical signs. Spayed female dogs are at increased risk for a UTI, which is likely due to anatomic differences as well as possible protective secretions from the prostate in sexually-intact males. Urinary tract infection (UTI) occurs when bacteria colonize portions of the urinary tract that are normally sterile (i.e., kidney, ureter, bladder, and proximal urethra). Ascent of bacteria is the most common origin of bacteria in UTI. Fecal flora from the patient contaminate the perineum, ascend the urethra, and enter the bladder. Organisms that successfully gain entry into the bladder then have the potential to ascend the ureters, cross the renal pelvic epithelium, and enter renal parenchymal tissue. Vaginal, preputial, and distal urethral flora occasionally are the source of ascending bacteria. Ascending organisms can also come from the environment including that from hospital flora. Introduction of normal flora during catheterization and contamination with fecal or hospital flora also is possible. Migration of bacteria around an indwelling urinary catheter or through the catheter lumen occurs at times.

The urinary tract is exquisitely resistant to bacterial colonization during health. UTI results from abrogation of one or more natural defense mechanisms that allow bacteria to ascend from the perineum to the urethra, and then to the bladder. The development of a UTI means that the host defenses were overwhelmed at least transiently in order for UTI to develop. In order for UTI to develop, the animal must be exposed to uropathogenic bacteria in sufficient numbers, the animal must have epithelial receptors for uropathogens, and often suboptimal urinary defenses exist. Failure of normal urinary defenses include the possibilities of reduced anti-adherence properties of the uroepithelium, decreased antibacterial properties of urine, abnormal patterns of voiding, reduced integrity of intrinsic mucosal defenses, and presence of anatomic abnormalities.

Increased risk for the development of UTI occurs in dogs with anatomic abnormalities of the genitourinary system such as urachal remnants, ectopic ureters, excessive perivulvar skin folds/pyoderma (especially in recurrent UTI), or possibly vestibulovaginal stenosis. Exogenous steroid use in dogs, endogenous hyperadrenocorticism, and diabetes mellitus all add risk for development of UTI in dogs. Urolithiasis can be the result of UTI (struvite stones in dogs) or the stones may compromise the urinary defense systems. Urethrostomy, indwelling urinary catheterization, and single passage of a urinary catheter increase the risk that UTI will be acquired in dogs and cats. UTI occurs in approximately 30% of all cats with chronic renal failure (CRF), many within one year of diagnosis of CRF. Cats over 10 years of age that present for signs of lower urinary tract distress (LUTD) commonly have bacterial urinary infections, unlike young cats presenting with LUTD signs. Dogs with urinary incontinence may be at increased risk for development of UTI possibly due to the “wicking” action of urine that may allow ascent of bacterial organisms.

**DIAGNOSING URINARY TRACT INFECTION**

Urinalysis and aerobic quantitative urine culture reported in colony-forming units per milliliter (cfu/mL) should be conducted in all pets suspected of having a UTI. The presence of bacteriuria and pyuria is highly suggestive of a UTI, but isolation of organisms in large quantitative growth (cfu/mL) is the gold standard for definitive diagnosis. In a recent study of dogs with UTI and urine samples collected by cystocentesis, 82% grew organisms at greater than $10^5$ cfu/mL, 6% from $10^4$ to $10^5$ cfu/mL, and 12% from $10^3$ to $10^4$ cfu/mL. The number of cfu/mL needed to definitively confirm the existence of UTI varies depending on how the urine is collected, whether it is collected from a dog or a cat, the animal’s sexual status, and whether clinical signs are present.

Urine collection by cystocentesis is the gold standard for definitively establishing a diagnosis of UTI since this method bypasses organisms that are often isolated from normal flora of the distal urethra or genitalia when collected by voiding or catheterization. Theoretically, no organism growth should occur in samples collected by cystocentesis. By convention, growth of more than 103 cfu/mL of an organism is required to exclude isolation of small numbers of contaminants from the skin during the procedure. Growth of organisms frequently occurs when urine samples are collected by midstream voiding from healthy dogs and cats, making this the least desirable method to obtain urine.
for quantitative culture. For this reason, culture of midstream voided urine samples cannot be used to reliably diagnose UTI in dogs. However, the degree of contamination is less for cats, so growth of more than 105 cfu/mL of an organism can be used to diagnose UTI in cats.

Culture of urine samples obtained following a single passage of a urinary catheter can be used to diagnose UTI in male dogs when more than 104 cfu/mL are isolated and in both male and female cats when more than 10^3 cfu/mL organisms are isolated. There is no level of cfu/mL that can be used to diagnose UTI in female dogs. By somewhat arbitrary convention in animals with indwelling urinary catheters, more than 10^3 cfu/mL or any number cfu/mL of the same organism isolated on sequential days is required to diagnose a UTI.

Results from susceptibility testing are also important as they can reveal the presence of resistance patterns to urinary antimicrobials that may predict treatment failure and the need for greater surveillance for a particular animal. A change in urinary antimicrobial may be needed based on the results of susceptibility testing after the initial treatment is started.

While a quantitative urine culture with susceptibility testing is the gold standard for diagnosis and treatment of a UTI, it can be costly, and in practice culture kits have been marketed for companion animal use. The Uricult Vet dip paddle system (LifeSign, Somerset, NJ) was recently reported to be a useful screening tool for identification of bacterial growth. Quantitative results (cfu/mL) determined by comparing growth on the paddles with a standard illustration of organism density provided by the manufacturer were not always accurate. Inaccuracy in identification of isolated organisms sometimes occurred when paddles were used, particularly when multiple uropathogens were present. This paddle system provides no method for susceptibility testing of isolated organisms, although the bacteria can be categorized into gram-positive or gram-negative status. When growth occurs, paddles or urine should be submitted to a commercial microbiology laboratory for identification and antimicrobial susceptibility testing. Veterinary hospitals should determine whether their referral microbiology laboratory will accept organisms already growing on paddles for definitive identification and minimum inhibitory concentration (MIC) testing. This paddle system for organism isolation appears most clinically useful as an in-house method to identify urine samples that are sterile or samples with low quantitative growth compatible with contamination during the sample collection.

**TREATMENT STRATEGIES**

Urinary antibacterials remain the hallmark for treatment of UTI, though correction of predisposing factors is also important. The concentration of antimicrobial that is achieved in the urine (micrograms/mL) is the most important factor in predicting eradication of UTI. Tissue levels of the antimicrobial will be important in those with renal and prostatic infections, as well as those with markedly thickened bladder walls from chronic infection. Antibacterial treatment for UTI is usually given for 7 to 14 days in those with uncomplicated UTI, at least 30 to 60 days for those with upper UTI, and for at least one month to sexually intact males. These guidelines for duration of treatment are based on conventional experience over the years, but surprisingly little data exist to support or refute these protocols. Ultimately, antimicrobials should be given for as long as is necessary to effect a bacteriologically sterile urine during administration of the medication and for a protracted time following discontinuation of the treatment. Antibacterials should be selected after confirmation of UTI by quantitative urinary culture. UTI can be treated on the basis of susceptibility testing, or on the basis of predicted biologic behavior in those with uncomplicated UTI.

The Working Group of the International Society for Companion Animal Infectious Diseases (ISCAID) recommends treatment with urinary antibacterial drugs that are likely to be effective against more than 90% of the urinary isolates when this information is available. In general, ISCAID recommends initial therapy for uncomplicated UTI with amoxicillin (11–15 mg/kg PO q8h) or trimethoprim–sulfonamide (15 mg/kg PO q12h); the group does not recommend amoxicillin–clavulanate for initial treatment in these cases due to lack of evidence for the need for clavulanate in addition to amoxicillin.

Empiric therapy should not be prescribed for patients with a complicated UTI (three or more per year), for patients whose infection was acquired in a hospital setting, for animals with no clinical signs, or for animals with a history of extensive antimicrobial use. Empiric treatment of UTI without use of culture and susceptibility testing is discouraged due to the increased likelihood of encountering multi-drug-resistant organisms in patients that have received prior therapy for UTI.

Seven to 14 days of an appropriate antimicrobial for treatment of an uncomplicated lower UTI is often recommended. At least 30 to 60 days of antimicrobial therapy is usually needed to sterilize chronic upper UTI (kidneys and ureters). Sometimes long-term bacteriologic cure is not possible.
Antibacterial treatment is usually required for a longer period of time in intact males with chronic prostatitis and UTI. These guidelines for treatment duration are based on conventional experience over the years, but surprisingly little data exist to support or refute these protocols. Ultimately, antimicrobials should be given for as long as is necessary to effect a bacteriologically sterile urine during administration of the medication and for a protracted time following discontinuation of treatment.

Most UTI can be successfully sterilized via the oral route using penicillins (especially those with clavulanate), trimethoprim-potentiated sulfonamides, ormetoprim-potentiated sulfonamides, or first generation cephalosporins such as cepahlexin or cefadroxil. Side effects associated with trimethoprim-potentiated sulfonamides include keratoconjunctivitis sicca, cytopenia, hepatopathy, and immune-mediated polyarthritis. Ormetoprim-potentiated sulfonamides are not effective in prostatic UTI. Trimethoprim-potentiated sulfonamides should be used in these cases. Sulfonamides of any kind should not be prescribed for those in which medical calculolytic protocols are in place. Sulfas can precipitate on the surface of the stone and either stop or dramatically decrease the rate of stone dissolution.

Fluoroquinolones such as norfloxacin, ciprofloxacin, enrofloxacin, orbifloxacin, marbofloxacin, and difloxacain provide oral treatment for resistant bacteria. The quinolones have a wide spectrum of antibacterial activity (except against enterococci and anaerobes), achieve high tissue concentrations, and are kidney-friendly. Difloxacain undergoes more hepatic excretion than the other fluoroquinolones, consequently less is excreted into urine. Fluoroquinolones should not be given to dogs that are still growing (less than 6 to 18 months of age depending on size/breed), due to the potential damaging effects on articular cartilage. The quinolones should be reserved for treatment when other therapeutic agents have failed unless there is compelling evidence that the organism in question is highly resistant to other antibacterial agents. An association between the use of enrofloxacin and blindness in some cats has been reported, with mydriasis often an early finding. All fluoroquinolones can create retinal lesions at higher doses. Although retinal toxicity is noted to be idiosyncratic in some cats, cats with renal or liver disease are at increased risk for toxicity, as reduced metabolism will result in higher plasma levels of fluoroquinolones and their metabolites. Reports of blindness in cats treated with enrofloxacin have decreased dramatically since the flexible dose range was redefined. A dose of 3 mg/kg once daily or 2.5 mg/kg twice daily is recommended in cats with renal or liver disease. IV fluoroquinolones should not be used in cats with liver or renal disease.

In a recent prospective double-blind clinical study, treatment of uncomplicated bacterial UTI in dogs was compared between a high-dose short duration (HDSD) course of enrofloxacin and a standard-duration regimen of amoxicillin–clavulanate. Excluded from the study were dogs with a history of persistent or recurrent UTI (defined as more than three UTIs in 1 year with or without a period of sterility), dogs with uncontrolled comorbid diseases or concurrent urinary problems such as calculi or neoplasia, and dogs that had recently received antimicrobials or glucocorticosteroids. Study dogs were randomized into one of two groups: Dogs in group 1 (n = 35) received enrofloxacin at 18 to 20 mg/kg PO q24h for 3 consecutive days, and dogs in group 2 (n = 33) received amoxicillin–clavulanate at 13.75 to 25 mg/kg PO q12h for 14 days. Urinalyses and urine cultures were submitted for dogs in both groups on days 0, 10, and 21. The microbiologic and clinical cure rates were compared between groups 7 days after completing the antimicrobial regimen (day 10 for group 1 and day 21 for group 2). The microbiologic cure rates were 77.1% and 81.2% for groups 1 and 2, respectively. Clinical cure rates were 88.6% and 87.9% for groups 1 and 2, respectively. Microbiologic and clinical cure rates between groups did not differ according to the selected margin of noninferiority. HDSD enrofloxacin treatment was not inferior to a conventional amoxicillin–clavulanate protocol for the treatment of uncomplicated bacterial UTI in dogs in this study.

Interestingly, three of the 35 dogs in group 1 were considered resistant to enrofloxacin based on serum achievable concentrations of enrofloxacin; clinical cure was achieved in all three of these dogs and microbiologic cure was achieved in two. Similarly, two of 33 dogs in group 2 were considered resistant to amoxicillin–clavulanate yet both achieved clinical and microbiologic cure. Some organisms that were susceptible to either enrofloxacin or amoxicillin–clavulanate based on MIC testing were not eradicated following treatment. Clinical signs persisted in the absence of UTI in some dogs and in other dogs UTI persisted in the absence of clinical signs, illustrating the importance of posttreatment quantitative urine culture.

These data suggest that the HDSD enrofloxacin protocol was similarly effective to the standard protocol of 14 days of amoxicillin–clavulanate in treating uncomplicated canine UTI in this sample patient population and may represent a viable alternative therapeutic regimen for similar
The SD protocol is not designed for use in dogs with complicated UTI (i.e., underlying anatomic or structural abnormalities, metabolic problems that result in dilute urine, or functional problems that adversely affect bladder and urethral function). Conventional treatment times and doses for enrofloxacin or another class of antibacterial should be prescribed for dogs with complicated UTI. Enrofloxacin can be given to dogs at the flexible dose range of 5 to 20 mg/kg q24h during conventional therapy depending on the identity of the isolated uropathogen and its resistance pattern. The HDSD treatment protocol should NOT BE USED IN CATS due to increased risk for retinal toxicity that can occur with all fluoroquinolones, especially at higher doses.10 The chances for young cats to have true bacterial UTI based on quantitative urine culture are very low. When enrofloxacin is given to cats the dose should not exceed 5 mg/kg q24h. It appears that cats more readily accumulate fluoroquinolone in the retina due to decreased egress mechanisms for this class of antibiotic compared with other species. The dose of this class of antibiotic should be reduced in those with poor kidney or liver function.

The urinary concentrations of enrofloxacin and ciprofloxacin (an active metabolite of enrofloxacin) far exceed the concentrations achieved in plasma. A single dose of oral enrofloxacin at 20 mg/kg achieved high levels of urinary enrofloxacin and even higher levels of urinary ciprofloxacin in a study of six healthy dogs.13 The mean maximal urinary concentration of enrofloxacin at any time was 139 μg/mL (range, 73–226 μg/mL); similarly, the mean maximal urinary concentration of ciprofloxacin was 371 μg/mL (range, 200–639 μg/mL). The average plasma concentration 2 hours following dosing was 3.4 μg/mL (range, 0.7–9.9 μg/mL) for enrofloxacin and 0.5 μg/mL (range, 0.18–0.96 μg/mL) for ciprofloxacin. The MIC for an average isolate of E. coli from dogs with uncomplicated UTI is often less than 0.25 μg/mL with enrofloxacin. Most discussions about enrofloxacin have not emphasized how much ciprofloxacin is generated for urinary excretion. Future decision making for likely urinary susceptibility to enrofloxacin should take into account the high levels of urinary ciprofloxacin generated following metabolism of enrofloxacin in addition to that of enrofloxacin. The use of oral ciprofloxacin in dogs is not recommended due to its low bioavailability in canine patients.14 All of the measured urine concentrations of ciprofloxacin at 2, 8, and 24 hours following administration of 20 mg/kg of enrofloxacin exceeded the mutant prevention concentration (MPC) for ciprofloxacin when tested against 28 urinary isolates of E. coli from canine patients in a pilot study at a veterinary college microbiology laboratory. The highest MPC for ciprofloxacin in these isolates was 1.0 μg/mL. These results are compatible with the hypothesis that HDSD protocols using enrofloxacin will delay the emergence of fluoroquinolone resistance among isolates of E. coli that cause UTI in dogs. Further studies in dogs with UTI treated with the HDSD enrofloxacin protocol are needed to determine whether this is true in the clinical setting by examining the resistance pattern of surviving organisms in the urinary tract that fail to be eradicated and evaluating the effects of this protocol on the resistance pattern of fecal flora.

Those that fail to get better (reduction in signs, pyuria, and quantitative urine culture results) or have multiple new positive cultures (with or without clinical signs) are by definition “difficult”. Animals that have received antibacterial treatment within the past two months are at increased risk that the organisms causing their UTI will be more resistant than from those who have not recently been exposed to antibiotics. Complicated cases have identifiable defects in host defense mechanisms, including anatomical, functional, or metabolic defects. They may have mucosal damage due to urolithiasis or neoplasia, alteration in urine volume or composition, be affected by a concurrent systemic disorder (diabetes mellitus, hyperadrenocorticism, neoplasia), or have received long-term exogenous steroids.

Recurrent infections are repeated episodes of bacterial urinary infection (positive quantitative urine culture often associated with clinical signs) usually following therapy. Recurrent infections are reinfections, relapsing infections, or persistent infections. Since treatment is so different, it is important to distinguish between recurrent infection that is due to reinfection, relapsing, or persistent infection. The only reliable way to do this is with quantitative urine cultures that are taken before treatment, while on antibiotics, and at various time intervals after treatment has been discontinued. Imaging studies are important in the evaluation of recurrent UTI (radiographs, contrast urography, ultrasonography, cystoscopy).

Reinfection is another clinical episode caused by a different organism than previously involved. This organism may be an entirely different genus and species, or may be the same, but a
different biotype (54% of recurrent UTI). This is a new infection that classically occurs weeks to months following discontinuation of drug therapy for a previous UTI. Multiple new infections suggest that the animal’s host defense mechanisms are not operating properly. A search for predisposing factors should be undertaken which includes anatomical defects, urolithiasis, urine retention (neurologic dysfunction), and neoplasia with disruption of urothelium.

No predisposing factors were found in 30% of dogs with recurrent UTI in one study, (Seguin, et al. 2003) indicating primary failure of defense mechanisms. Predisposing factors for recurrent UTI were identified in 70% of these dogs of which about 1/3 could be corrected. Nearly 30% of the isolates from this study were resistant to achievable plasma concentrations of commonly prescribed oral antibacterials.

In some instances, dogs with reinfections will have moderate to severe recession of the vulva due to overlying skin folds or cranial displacement of the vulva. It appears that this type of vulvar recession is a risk factor in dogs prone to UTI (many without UTI also have vulvar recession). The flora and or number of organisms near the vulva likely favors increased ascent of bacteria; the recessed vulva may also serve as a barrier to the complete emptying of urine which can contribute to incontinence or ascending infection due to wicking of bacteria. Recent reports attest to the success of vulvoplasty or episiotomy in dramatically reducing the recurrence of UTI in these individuals. This risk factor is frequently overlooked by primary care veterinarians and also internists and surgeons.

The syndrome of so-called “vestibulo-vaginal stenosis” has been implicated as an underlying cause for recurrent UTI and urinary incontinence. We remain skeptical about the reality of this diagnosis, as we have failed to confirm this condition during cystoscopy in hundreds of female dogs with a variety of lower urinary tract conditions. There is tremendous variation in the normal diameter of the vestibulo-vaginal junction – varying with sexual status and the conditions of vaginography. Digital palpation of the vestibule is not reliable to establish this diagnosis. Studies employing CT vaginography and cystoscopy to make precise measurements indicate wide variability in the normal appearance and measurement of these structures (Wangs and Samii). We advise caution in the use of any aggressive surgical correction of vestibulo-vaginal stenosis. It is our opinion that vestibulo-vaginal stenosis is often diagnosed in the referral community.

Relapsing infection is another clinical episode caused by the same identical organism (same serotype) and implies persistence of an organism that was never eradicated (44% of recurrent UTI). This suggests that the infection is deep-seated within the tissues or that the organisms are resistant to the chosen antibiacteral. Clinical signs tend to occur soon following discontinuation of medications, usually within days to a week.

Persistent UTI is a variant of relapsing infection in which bacterial cultures remain positive with the same organism during antibacterial treatment. In this instance it has never been possible to eradicate the organism even transiently. Persistent infection occurs in approximately 2% of all recurrent UTI and implies severe abrogation of local host defenses, or that the organism is highly resistant to the present antimicrobial agent. A search for predisposing factors should be undertaken to exclude pyelonephritis and obstructive nephropathy, urolithiasis, chronic bladder wall changes allowing sequestration of bacteria anatomical defects, polypoid cystitis, urine retention, and prostatic or uterine reinoculation from bacterial prostatitis or metritis.

Female dogs typically have recurrent infections with Staphylococcus, Enterococcus sp., or Pseudomonas. Male dogs with recurrent UTI are more likely to have Klebsiella, Providencia, Salmonella sp., Corynebacterium sp., Acinetobacter sp., and Actinomycetes sp. In recurrent infections, 20% of dogs have two bacterial organisms isolated, and 4% have three isolated.

Long-term medication is not usually indicated for those with reinfection forms of UTI, since routine therapy will eradicate the present infection. Most of the time, predisposing factors will not be found despite intensive investigation. The present infection is usually easily eradicated, but it often recurs in subsequent months. The organisms associated with reinfections are not usually those with high resistance patterns to urinary antibacterials. Though no studies have been reported on the effectiveness of these protocols, prophylactic therapy can be useful to prevent new infections after the previous infection has been sterilized in patients that have had multiple incidents of UTI. Subtherapeutic doses of antimicrobials are given, but often successfully prevent the development of new UTI. This may allow the host’s defense systems to handle reduced numbers of bacteria. Bacteria that are not directly killed by the antimicrobial may not express the fimbria necessary to attach to the urothelium, and consequently are readily flushed away during voiding. An appropriate antimicrobial is administered in the standard manner and then is followed by the chronic administration of 1/3 to 1/2 of the total daily dosage given once daily. It is recommended that the owner give the medication at
bedtime. This maintains high levels of the excreted antimicrobial within the urine, obtaining a maximal prophylactic effect. Trimethoprim-potentiated sulfonamide, cephalexin, or nitrofurantoin is recommended if the UTI has a Gram-negative etiology. Ampicillin/clavulanate or trimethoprim-potentiated sulfonamide is effective when the UTI is associated with Gram-positive bacteria. Fluoroquinolones may be given for prophylaxis if the UTI has been associated with highly resistant organisms. It may be best to use the antibiotic for prophylaxis that most recently resulted in clearance of the UTI using full therapeutic doses. Prophylaxis may be necessary for at least six consecutive months to prevent reinfections. Ideally, the urine should be cultured monthly to ensure that the urine remains sterile. If the urine remains sterile for 6 months, the animal’s urinary defense mechanisms may have improved, and further medication may no longer be needed.

By definition, relapsing UTI means that we have never fully eradicated the organism from the urinary tract, either because the organisms are inaccessible, not enough antimicrobial is concentrating in the urinary tract, or that the organisms are highly resistant to the chosen antibacterial. Long-term therapy with an appropriate antibiotic for 30 to 60 days or longer may be necessary. Susceptibility testing preferably with methods that report MIC should be performed to ensure selection of an antibiotic with a chance to eradicate the organism. Change of antibiotic class may be needed to one that achieves greater tissue penetration such as that which is achieved with the use of fluoroquinolones. It is essential to make sure that predisposing anatomical factors (urolithiasis, polypoid cystitis, urachal remnants) that allow sequestration of bacteria have been eliminated. Culture of urine while the animal is receiving antimicrobials is recommended as an in-vivo method of susceptibility testing. There is no chance for bacterial eradication if organisms continue to grow in urine while being treated with antibacterials.

By definition, persistent UTI is associated with bacterial organisms that continue to grow in urine from patients that are receiving antibacterials. This is the worst case scenario of those with recurrent UTI. The fact that urine cannot be sterilized while on antibacterials indicates treatment failure. This occurs when the organisms are resistant to the chosen antibacterial, when the antibacterial does not accumulate in high enough concentration to inhibit the organism (such as in patients with reduced renal function), when the organisms are inaccessible, or when the host urinary defenses are severely compromised.

More potent antibacterials should be chosen if the organism is resistant to first line antibacterials initially or the MIC increases during treatment to levels beyond that than can be achieved by the present antibacterial. Antibiotics that have greater tissue penetration may be needed in those with chronic inflammatory and scarring changes of cystitis or pyelonephritis. Aminoglycosides (gentamicin, amikacin) should be reserved for highly resistant bacteria, or those that have failed to respond to aggressive treatment with other antibacterials. Aminoglycosides can be nephrotoxic, and are available only via injection. If needed, less nephrotoxicity is encountered if the daily dose is given all at once rather than divided throughout the day. Cefditoren sodium is a third generation cephalosporin labeled for treatment of dogs with UTI and can be effective in the eradication of UTI when given by once daily injection. Ceftiofur has good activity against E. coli and Proteus, but possesses little activity against Pseudomonas or Enterococcus. Cefizime (Suprax® tablets & suspension) is a third generation oral cephalosporin that is useful for the treatment of resistant infections, but it is very expensive. Methenamine is an older antiseptic drug that can be useful in the treatment of E. coli UTI that is resistant to the fluoroquinolones. Methenamine is metabolized to formaldehyde which kills bacteria, but it requires highly acid urine for this effect. Meropenem and imipenem can be used for selected cases of UTI with highly resistant bacteria — they should not be used for routine UTI.

Successful treatment depends on the presence of sterile urine during and after medication. Resolution of clinical signs, hematuria, proteinuria, and microscopic bacteriuria can be misleading, since these can occur from reduced activity of the UTI, but not necessarily its eradication. Quantitative urine cultures are recommended 5 to 7 days, 1 month, and 3 months after medication has been discontinued to ensure that sterility within the urinary tract has been maintained. For recurrent cases of UTI, quantitative culture of urine during treatment can be quite helpful (See Tables).

Cranberry juice or extract may be effective to reduce the frequency of recurrent UTI due to new infections in some humans following initial eradication of UTI with antimicrobial drugs. This beneficial effect has been attributed to impairment of bacterial adherence to uroepithelium by proanthocyanidins (PAC) found in cranberries; this effect may be more specifically directed against attachment of P-fimbriated E. coli to uroepithelium. Adherence to uroepithelium is an initial first step in colonization and further growth resulting in the establishment of UTI. Anti-adherence properties against uropathogenic E. coli were demonstrated in two studies using urine from dogs treated with
cranberry extract. Urine collected from female dogs treated for 30 days with cranberry extract showed a 30% decrease in adherence of \textit{E. coli} using cell cultures from Madin-Darby Canine Kidney (MDCK) cells compared to urine before treatment (Smee JVIM 2011). Male dogs were treated daily for 3 weeks with cranberry extract in a second study using an assay designed to demonstrate the ability of P-fimbriated \textit{E. coli} to agglutinate human red blood cells. Anti-adhesion activity was demonstrated in the urine of these dogs within three hours following treatment with cranberry extract and the peak effect was reached by 7 days (Howell JVIM 2010). Both of these studies used surrogates for attachment of uropathogenic \textit{E. coli} to uroepithelium in clinical patients. Studies demonstrating the ability of cranberry extract to reduce the frequency of recurrent UTI in dogs have yet to be published. Moreover, the degree to which uropathogenic \textit{E. coli} contribute to the overall incidence of UTI in dogs is unknown, and the effect of cranberry therapy on pathogens lacking P-fimbriae (e.g. \textit{Staphylococcus} spp., \textit{Enterococcus} spp., \textit{Proteus} spp.) is also unknown.

SELECTED READING


Figure 1. Uropathogenic Escherichia coli and uroepithelial cell. Structure with pili, adhesins, and virulence factors. Adhesins on the end of the fimbria facilitate binding to specific receptors on the uroepithelial cells. 1, Supercoiled bacterial DNA; 2, Lipopolysaccharide (LPS) of bacterial wall; 3, 4, and 6, Fimbria without adhesins that fit into uroepithelial cells; 5, Fimbria with adhesins that specifically fit into the uroepithelial receptors-binding with these receptors is pivotal in allowing the establishment of UTI; 7, Flagellum; 8, Various virulence factors produced by the organisms that favor pathogenicity. (Drawn by Tim Vojt—From Canine and Feline Nephrology and Urology, edited by Chew DJ, DiBartola SP and Schenck PA; Elsevier 2010)
Figure 2. Bacteria Associated with UTI in Dogs – 2000 to 2007. Courtesy of the Microbiology Laboratory of The Ohio State University College of Veterinary Medicine.

Figure 3. Bacteria associated with UTI in Cats - 2000 to 2007. Courtesy of the Microbiology Laboratory of The Ohio State University College of Veterinary Medicine.

Figure 4. Quantitative Growth of *E. coli* in large numbers after incubation of urine collected by cystocentesis for 24 hours - > 30,000 cfu/ml. Using a 1µl or 10µl (shown below)
calibrated loop, an estimate of bacterial concentration in urine in cfu/ml can be made by multiplying the number of colonies on the plate by a dilution factor of 1,000 or 100. The plate above contains > 300 cfu, which is too high to count accurately. Nonetheless, because there are more than 10 colonies on the plate, it is clinically significant for a cystocentesis-derived sample.

Table 3. Functional/anatomical abnormalities predisposing to or perpetuating UTI (Complicated UTI)
- Deep-seated cystitis (chronic wall changes)
- Pyelonephritis
- Prostatitis (sexually-intact)
- Metritis/pyometra
- Neoplasia – bladder/urethra
- Small urinary calculi – previously missed
- Urachal remnant (developmental)
- Peri-urachal microabscesses
- Ectopic ureters (developmental)
- Urethral sphincteral incompetence with incontinence
- Polypoid cystitis
- Poor vulvar conformation/development
- Vestibulovaginal stenosis (developmental)
- Ureterocoele
- Bladder atony (residual urine volume)
- Neurogenic bladder/urethra
- Detrusor-urethral dyssynergia
- Urethral stricture
- Urethral fistula or other anomalous pattern

Table 4. Metabolic conditions predisposing to or perpetuating UTI
- Diabetes mellitus
- Hyperadrenocorticism
- Exogenous steroid administration
- Renal Failure (especially cats)
- Hyperthyroidism
- Immunosuppression/chemotherapy

Table 5. Likelihood for diagnosis of a true bacterial UTI based on quantitative growth and the method of urine collection.
<table>
<thead>
<tr>
<th>Culture method</th>
<th>Contamination (cfu/ml)</th>
<th>Infection (cfu/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Midstream voided</td>
<td>&lt; 10⁶</td>
<td>&gt; 10⁶ in cats; cannot distinguish in dogs</td>
</tr>
<tr>
<td>Catheterized</td>
<td>&lt; 10⁷ in male dogs and all cats; any number in female dogs</td>
<td>&gt; 10⁷ in male dogs &gt; 10³ in cats &gt; 10² or any number on sequential days in animals with indwelling catheters</td>
</tr>
<tr>
<td>Cystocentesis</td>
<td>&lt; 10⁷ (be skeptical)</td>
<td>&gt; 10⁶</td>
</tr>
</tbody>
</table>

Table adapted from Greene et al. Infectious Diseases of the Dog and Cat, 2006. p. 946

Table 6. **Schedule of urine cultures for difficult recurrent cases.** Recheck cultures should never be taken by urinary catheter, as it is impossible to perform a sterile catheterization because of distal urethral flora and the propensity for vaginal contamination during this procedure.

<table>
<thead>
<tr>
<th>Initially</th>
<th>Document organism and susceptibility</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 to 5 Days on Treatment</td>
<td>Document effective eradication in urine</td>
</tr>
<tr>
<td></td>
<td>Rule out persistent infection</td>
</tr>
<tr>
<td></td>
<td>Change in MIC if persistent?</td>
</tr>
<tr>
<td></td>
<td>Rapid emergence of resistance?</td>
</tr>
<tr>
<td>3 days before treatment ends</td>
<td>Rule out superinfection – rare</td>
</tr>
<tr>
<td>(new organisms identified?)</td>
<td></td>
</tr>
<tr>
<td>7 to 10 days after treatment ends</td>
<td>Rule out relapse</td>
</tr>
<tr>
<td>1, 2, 3, 6, 12 months after treatment</td>
<td>Identify reinfections</td>
</tr>
</tbody>
</table>

Table 5. Summary tips recommended for approach to UTI

<table>
<thead>
<tr>
<th>DOs</th>
<th>DON’Ts</th>
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<tbody>
<tr>
<td></td>
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<tr>
<td><strong>Culture urine in all dogs and cats with signs of lower urinary tract disease.</strong></td>
<td>Don’t blindly pick an antibacterial agent unless financial constraints of the owner dictate otherwise.</td>
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<tr>
<td>Collect urine by cystocentesis for culture.</td>
<td>Don’t culture voided urine.</td>
</tr>
<tr>
<td>Periodically culture urine from cats with CRF, from dogs and cats receiving corticosteroids, and from those with diabetes mellitus or hyperadrenocorticim.</td>
<td>Don’t ignore the likelihood of UTI in patients with CRF, diabetes mellitus, and hyperadrenocorticim. UTI in such patients often is often asymptomatic.</td>
</tr>
<tr>
<td>Perform a direct examination of fresh urine; culture the urine.</td>
<td>Don’t assume urine is sterile if bacteria are not seen in urine sediment. Don’t assume that “bacteria” in sediment are real, especially in the absence of pyuria.</td>
</tr>
<tr>
<td>Use urine sediment examination to visualize WBCs.</td>
<td>Don’t depend on dipsticks to detect WBCs in urine. They are unreliable in dogs and cats.</td>
</tr>
<tr>
<td>Perform urinary catheterization when medically or surgically necessary, but be aware of the risk of introducing UTI.</td>
<td>Don’t ignore the risk of UTI after urinary catheterization. Don’t carelessly administer antibiotics to animals with indwelling urinary catheters. Infection may be delayed but not prevented, and resistant organisms are likely.</td>
</tr>
<tr>
<td>Culture urine after treatment to ensure sterility of urine.</td>
<td>Don’t rely on resolution of clinical signs to indicate that urine is sterile.</td>
</tr>
<tr>
<td>Follow a full course of antibacterial therapy.</td>
<td>Don’t discontinue treatment early just because the patient looks or feels better.</td>
</tr>
<tr>
<td>Treat all cases of UTI, even those that are asymptomatic.</td>
<td>Don’t ignore the potential consequences of untreated UTI.</td>
</tr>
</tbody>
</table>
"Pearls" - Urinary Tract Infection (UTI) – Dennis J. Chew DVM Dipl ACVIM

1. E. coli, followed by Staph and Proteus account for most cases of UTI.

2. UTI is a disease of dogs. The diagnosis of UTI in cats is very frequently WRONG unless the cat has very specific risk factors to acquire UTI.

3. Quantitative urine culture is needed to know for sure that UTI is real. Bacterial growth is reported in cfu/ml rather than positive, or mild, moderate, large growth.

4. Though you may find it hard to believe, MOST UTI in the dog are not associated with clinical signs. Many dogs seem to live without realizing that they harbor bacterial organisms in the bladder.

5. Treatment of UTI is best based on results of susceptibility testing – preferably based on MIC.
6. Time honored tradition suggests that dogs should be treated for their UTI for 7 to 21 days. There is no data to support the time frame needed to sterilize the urinary tract.

7. It is best to PROVE that UTI has been eradicated by culturing the urine again 5 to 7 days after antibacterial medications have been discontinued.

8. Microbiological sterility and clinical cure are NOT the same endpoints.

9. Amoxicillin and Sulfa-TMP are favored as first choices in the treatment of UTI by the ISCAID.

10. There is no evidence that amoxicillin-clavulanate is superior to amoxicillin alone – ISCAID.

11. A relatively new treatment regimen for UNCOMPLICATED UTI in dogs was published in 2012. It is referred to as the HDSD study (High Dose Short Duration) in which about 20 mg/kg of enrofloxacin once daily for 3 days was found to be “not inferior” to 14 days of amoxicillin-clavulanate given twice daily.

12. About 80% of seemingly uncomplicated UTI in dogs can be expected to respond to treatment with either HDSD enrofloxacin or regular dosing of amoxicillin-clavulanate.

13. When UTI fails to respond to initial treatment, it is helpful to decide if the UTI is a reinfection (new bug) vs relapsing (same bug that never really went away).

14. A commonly overlooked predisposition for the reinfection is that of vulvar conformational problems that provide “hooding” of the vulva. Episioplasty can be helpful in preventing such recurrences.

15. Proanthocyanidins (PAC) in cranberry extract have the potential to inhibit recurrent UTI due to some organisms. In vitro laboratory testing provides support that this treatment strategy COULD work, but evidence in dogs showing reduced frequency of recurrent UTI has yet to be published.

16. In those with recurrent UTI, it is essential to look for anatomical (diverticulum, ectopic ureter, vulvar conformation), metabolic (CKD, diabetes mellitus, Cushing’s disease), and functional (incomplete bladder emptying, urinary incontinence) abnormalities that allow new infections to develop or that prevent current infections from being eradicated.

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