Treatment of urinary tract infection (UTI):
Guidelines for sporadic and recurrent UTI

Larry G. Adams, DVM, PhD, Diplomate ACVIM (SAIM)
Purdue University College of Veterinary Medicine, West Lafayette, Indiana

Classification of bacterial cystitis

Bacterial cystitis can be classified according to several definitions. *Sporadic bacterial cystitis* is defined as bacterial infection in the bladder results in inflammation resulting in clinical signs such as pollakiuria, stranguria, dysuria and hematuria.¹ Sporadic bacterial cystitis mainly occurs in otherwise healthy, non-pregnant females and less commonly in castrated males. Comorbidities such as uroliths, neurologic disease (IVDD) or endocrinopathies (diabetes mellitus, hyperadrenocorticism) are rarely present in this group. Sporadic bacterial cystitis was previously referred to as simple uncomplicated lower UTI; however, the International Society of Companion Animal Infectious Diseases (ISCAID) Guidelines discourage the use of this term because it is often difficult to determine if the UTI is truly uncomplicated in dogs.

Dogs with more than 3 UTIs within 12 months are classified as having recurrent urinary tract infections (UTI). Recurrent UTIs are common in dogs.¹⁻³ There are 2 major types of UTI recurrence: relapse and reinfection.³ The implications of relapse versus reinfection are important for management of recurrent UTI. Relapses are defined as UTI recurrence of the same species and strain of microorganisms within days to weeks of completion of therapy accompanied by clinical signs of either pyelonephritis or lower urinary tract signs (LUTS). Reinfections are recurrent UTI caused microorganisms that are different than the prior UTI.

*Subclinical bacteriuria* (SBU) is a term used in human medicine (also called asymptomatic bacteriuria) to describe the presence of bacteria in the urine, as determined by a positive bacterial culture, in the absence of LUTS. Subclinical bacteriuria (SBU) also occurs in dogs and cats.⁴⁻⁷ Subtle LUTS may be difficult to discern in small animals, so the distinction between SBU and UTI per se is not always easily defined. Subclinical bacteriuria has been variably reported in dogs and cats with prevalence rates in cats reported from 1% -29%.⁴⁻⁷ In one study evaluating 101 healthy adult dogs, SBU was present in 8.9% of the dogs.⁴ Cats with SBU are typically older, female cats.⁵,⁶ Subclinical bacteriuria is also anecdotally reported more often in animals with endocrinopathies, chronic kidney disease (CKD), in animals treated with glucocorticoids or immunosuppressive agents, or in cats that have altered anatomy from perineal urethrostomy. Deciding if or how to treat SBU in dogs and cats is often challenging. Treatment of SBU is not usually indicated (see below).

*Pyelonephritis* is defined as an infection of the renal pelvis and surrounding renal parenchyma and is also referred to as upper UTI.⁷ Differentiation of pyelonephritis from lower UTI alone is not always easy determined.

Causes of recurrent UTI

Most UTIs occur from ascending bacterial infection from the vaginal vestibule or prepuce. There are normal host defenses that protect the urinary tract from ascending
infection. Interference with normal host defenses may contribute to recurrent ascending infections. Potential contributing factors include urinary incontinence, incomplete voiding, urine stasis or reflux, disruption of or damage to the urothelium (urothelial carcinoma), anatomic abnormalities, morbid obesity, perivulvar dermatitis, alterations in immune competence, alterations of urine composition (glucosuria), or iatrogenic causes (perineal urethrostomy, indwelling urinary catheters). Young adult cats rarely have bacterial UTI unless prior procedures (e.g., indwelling urinary catheters) predispose them to acquired UTI; older cats are more commonly affected by UTI (or SBU) because of concurrent diseases such as CKD, diabetes mellitus and hyperthyroidism that cause dilute urine or impaired immune competence.

Common causes of UTI relapse include inappropriate antibiotic use (incorrect antibiotic dose, duration, or poor owner compliance), persistence of infection within a nidus in the urinary tract (urooliths, neoplasia, pyelonephritis, prostatitis), and emergence of drug-resistant pathogens. Common causes of reinfection include failure to eliminate predisposing causes for UTI (perivulvar hooing with perivulvar dermatitis, vaginal septa), urinary incontinence, and systemic illness (e.g., CKD, diabetes mellitus and hyperadrenocorticism). A rare cause of UTI is recto-urethral fistula, which presents usually with reinfections and multi-organism infections. Bulldogs are the most commonly reported breed for recto-urethral fistulas.

**Diagnostics for sporadic bacterial cystitis**

For sporadic cystitis, urinalysis with quantitative aerobic urine culture of urine obtained by cystocentesis is recommended including antimicrobial susceptibility testing of any pathogen(s) isolated. The presence of more than $10^3$ cfu/mL of bacteria is considered clinically significant for urine specimens collected by cystocentesis. If the urine is well concentrated and glucosuria is absent, then further diagnostics, such as complete blood count (CBC), serum biochemical panel, and imaging studies, are not usually warranted in an otherwise healthy animal if the suspected infection is an isolated event. We are currently evaluating voided urine with and without perivulvar cleansing in female dogs as an alternative to cystocentesis, which may be useful for dogs with concurrent illness that makes cystocentesis less idea (e.g., urothelial carcinoma).

**Diagnostic approach to animals with recurrent UTI**

The standard diagnostic evaluation for dogs with recurrent UTI should include history, physical examination, CBC, serum biochemistry profile, urinalysis, urine culture, abdominal radiographs and ultrasound (if available). The history should be reviewed to assess client compliance with prior treatments, diseases or drugs that could contribute to immunosuppression, evidence of urinary incontinence, or skin issues including perivulvar dermatitis. Physical examination should include careful examination of the vulva and perivulvar skin for evidence of recessed or “hooded” vulva with perivulvar dermatitis that may contribute to reinfection of the urinary tract. Rectal examination should also be included as a standard part of the physical examination of dogs to evaluate the urethra for masses or uroliths that could contribute to recurrent UTI. Abdominal radiographs should include the entire urinary tract including both kidneys and the entire urethra caudal to the pelvis.
Cystoscopy is recommended for diagnostic evaluation for dogs with recurrent UTI if an underlying cause has not been identified during initial work-up. Cystoscopy helps rule out anatomic abnormalities, polyps, neoplasia or uroliths and permits mucosal biopsy for culture, cytology and histopathology. Results of culture of bladder mucosa have yielded conflicting results in some studies.

Cultures of tissue or uroliths are more sensitive than routine urine culture for detecting chronic UTI especially in dogs previously treated with antibiotics. Bacteria were isolated from bladder mucosal cultures or urolith cultures in 18 to 24% of dogs despite concurrent negative urine cultures. Cultures of mucosal biopsies are readily obtained during cystoscopy. One study did not find an advantage of culture of cystoscopic biopsies compared to urine culture. However, clinical experience suggests benefit of such cultures in selected cases. Cytology and histopathology of cystoscopic biopsies are required to differentiate benign polyps and polypoid cystitis from neoplasia (most commonly urothelial carcinoma). Correction of anatomic abnormalities (ectopic ureters, vaginal septal remnants) detected during cystoscopy may help prevent recurrent UTI.

**Treatment of sporadic cystitis**

Imitating antimicrobial therapy while awaiting culture results is most commonly recommended for dogs with sporadic cystitis. There is evidence from humans that analgesics alone may be as effective as antimicrobials in uncomplicated bacterial cystitis; therefore, administration of NSAIDs pending urine culture results is an alternative approach to initiating empirical antimicrobial therapy. For empirical therapy, the ISCAID Guidelines recommend amoxicillin as a reasonable first choice in most areas unless there is prior documentation of high frequency of bacterial resistance to amoxicillin. While amoxicillin/clavulanic acid is also reasonable first tier antibiotic, evidence of benefit of clavulanic acid for treatment of UTI is lacking, even in UTIs with beta-lactamase producing bacteria, because high urinary concentrations of amoxicillin are usually achieved in animals with good renal function. (Some pharmacologists also suggest that urinary excretion of clavulanic acid is limited.) Trimethoprim-sulfonamide is another first tier option, but may be associated with greater adverse effects in some dogs. However, the likelihood of adverse effects on first exposure is low with short courses of therapy recommended by ISCAID. Treatment for 3-5 days for sporadic bacterial cystitis is recommended in most cases as opposed to prior recommendations of 10-14 days. Although one study documented that high dose short duration enrofloxacin was effective for sporadic cystitis, fluoroquinolones should be reserved for patients with documented need to this class of antibiotics or for animals with suspected pyelonephritis. Treatment should be based on clinical cure, rather than microbiological cure; therefore, follow-up urine cultures are not recommended for animals with sporadic cystitis.

**Diagnostic and therapeutic approach for animals with recurrent UTI**

Treatment of recurrent UTI should include diagnostics to obtain a specific diagnosis followed by a systematic treatment approach. Treatment of recurrent UTI should be based on aerobic culture and sensitivity testing of urine samples obtained by cystocentesis (or from culture of mucosal biopsies) rather than empiric antimicrobial
therapy. Pending urine culture results, administration of NSAIDs may be considered to minimize clinical signs until culture results are available to guide antibiotic selection. By convention, treatment for dogs and cats with recurrent UTI has been recommended for up to 4 weeks, but a shorter course of therapy (10-14 days) is likely effective in these cases as well. (For re-infection rather than relapse, a short course of 3-5 days may be adequate.) The clinician can consider obtaining a urine culture shortly after beginning the drug regimen and again 7 days after completing the antimicrobial. If a positive culture is found, further diagnostic tests to investigate for underlying comorbidities should be performed. Treatment should be based on clinical cure, rather than microbiological cure. Therefore, follow-up urine cultures obtained after completion of antibiotics are not considered essential based on the ISCAID Guidelines.¹

Urine cultures obtained during antibiotic therapy prove in vivo efficacy of the drug selected on the basis of the initial in vitro susceptibility testing. This culture will be positive in dogs that have persistent infections that may show in vitro susceptibility to the administered antibiotics, yet treatment fails to resolve the resistant infection. Positive cultures during antibiotic treatment may necessitate change of the antibiotic treatment especially in animals in which the clinical signs have not improved.

Episioplasty may be effective for resolving re-infections that occur secondary to perivulvar dermatitis.¹⁸ Weight loss and control of active UTI are also recommended prior to episioplasty. Resolution of relapsing UTI secondary to infected uroliths usually requires removal of the uroliths in order to achieve resolution of the UTI. Urinary incontinence may also contribute to recurrent UTI: if urine can leak out of the bladder, then bacteria may be able to ascend through the urethra from the lack of a tight seal. Effective treatment of urinary incontinence may reduce the risk of recurrent UTI in dogs. For dogs with vaginal septal remnants, laser transection of the remnant may be beneficial to preventing future ascending UTIs.¹³

**Diagnosis and treatment of pyelonephritis**

Bacterial pyelonephritis usually results from ascending infection, but less commonly occurs from hematogenous spread of bacteria to the renal parenchyma and pelvis. Clinical signs and physical examination findings of pyelonephritis may include fever, lethargy, anorexia, polyuria, polydipsia, pain upon kidney palpation, and other signs associated with acute kidney injury (AKI). A diagnosis of pyelonephritis can be suspected based on positive aerobic bacterial urine culture when accompanied by these clinical signs, as well as clinical laboratory findings of azotemia, pyuria, cylindruria, and neutrophilic leukocytosis with left shift and toxic neutrophils; and suggestive ultrasonographic findings such as renal pelvic dilation, blunting of the renal papilla and increased echogenicity of the deep renal medulla. These ultrasonographic findings are not pathognomonic for pyelonephritis and renal pelvic dilation can be noted in patients with (pathologic or physiologic) diuresis and with early ureteral obstructions. Pyonephrosis, a collection of sloughed urothelium and inflammatory cells in the dilated renal collecting system is a complication that can be caused by partial or complete ureteral obstruction with concurrent upper UTI. The diagnosis of pyelonephritis can be challenging clinically. Definitive diagnosis of pyelonephritis is not required and sometimes the clinical diagnosis is made retrospectively based on resolution of clinical
signs. Ultrasound-guided nephropyelocentesis can be safely performed to obtain urine for culture, but this is not usually required for effective treatment of pyelonephritis.

For treatment of animals with pyelonephritis, empirical antibiotic therapy should be initiated pending urine culture results rather than waiting for culture results. Urine should be obtained for urine culture before the first dose of antibiotics. For stable dogs or cats with suspected pyelonephritis that are clinically well, eating normally and have normal renal parameters, orally administered antibiotics are adequate. For unstable or azotemic patients, intravenous antibiotics should be initiated for the first 2-3 days, then transitioned to oral antibiotics once the patient is improved and culture results are available. Initial treatment should involve antimicrobial drugs known to have efficacy against Enterobacteriaceae, based on the predominance of those organisms in pyelonephritis. Based on the ISCAID Guidelines, treatment with a fluoroquinolone excreted in urine in the active form is a reasonable first choice for pyelonephritis. The author prefers oral pradofloxacin in cats to reduce the risk of blindness from other fluoroquinolones. Once culture and susceptibility results are available, treatment should be revised if necessary. Treatment for 4-6 weeks was previously recommended for veterinary patients with pyelonephritis. However, shorter duration therapy has been investigated in humans with pyelonephritis and should be considered in veterinary patients. While the ISCAID Guidelines recommend 10-14 day duration of antibiotics for treatment of pyelonephritis, the author prefers administration of antibiotics for 3 (or 4) weeks based on clinical experience of treatment failures with shorter courses of antibiotics. Follow-up evaluation should include physical examination, monitoring of renal values, urinalysis and urine culture 1 week after completion of antibiotic therapy to confirm resolution of pyelonephritis. The significance of a positive urine culture must be interpreted in light of the patient’s clinical response and renal function. If the patient’s clinical signs have resolved and renal function is improved/stable, then a positive urine culture could indicate either persistent pyelonephritis or subclinical bacteriuria (SBU). The ISCAID Guidelines suggest managing such patients similar to SBU with monitoring of renal function over time.

For patients with pyonephrosis, it is important to establish drainage of the renal pelvis typically by placement of a ureteral stent combined with appropriate antimicrobial therapy. The most common clinical scenario causing obstructive pyonephrosis is infected nephroliths or ureteroliths. Dissolution of obstructive struvite ureteroliths is possible using ureteral stent placement, antibiotics and struvite dissolution dietary therapy.

**Diagnosis and treatment of prostatitis**

Diagnosis of prostatitis is made based on the finding of culture confirmed UTI, suggestive ultrasonographic changes in the prostate and compatible clinical signs. Clinical signs include fever, pain on rectal palpation of the prostate, accompanied by LUTS in most dogs. Results of CBC may also show neutrophilic leukocytosis with left shift and toxic neutrophils. Intact male dogs with UTI without overt signs of prostatitis should still be assumed to have infection of the prostate; therefore, antibiotics selected for treatment of UTI in intact male dogs should achieve good prostate penetration. Examples of antibiotics with poor prostate penetration include penicillin, ampicillin, amoxicillin-clavulanic acid, cephalosporins, and aminoglycosides. Antibiotics that
achieve good prostate concentration and are more likely to be effective for treatment of UTI complicated by bacterial prostatitis in dogs include fluoroquinolones (enrofloxacin, marbofloxacin, and pradofloxacin), trimethoprim-sulfa, and potentially chloramphenicol. Bactericidal antibiotics such as fluoroquinolones are generally preferred over bacteriostatic antibiotics for treatment of chronic prostatitis. Duration of antibiotic therapy for prostatitis in dogs is not definitively known. For acute prostatitis, 4 weeks of antibiotics combined with castration may be adequate. For chronic prostatitis, 4-6 weeks or treatment is recommended along with castration. Prostatic abscesses should be aggressively managed with intravenous antibiotics initially, surgical omentalization, castration and 4-6 weeks of oral antibiotics.

**Adjunct treatment for recurrent UTI**

Alternative approaches for prevention and treatment of recurrent bacterial cystitis that have been investigated in human beings as well as animal models include the use of cranberry extract. The efficacy of cranberry extract in women has been mixed, but a recent metaanalysis showed that cranberry extract may reduce recurrent UTI in otherwise healthy women. While cranberry has been shown to prevent adherence of *E. coli* strains in *in vitro* studies, one study in dogs with intervertebral disk disease did not appear to reduce the risk of UTI in that placebo controlled trial. Live biotherapeutic products appear promising for treatment of recurrent UTI in humans and dogs. Intravesicular administration of nonpathogenic *E. coli* ASB 83972 in human beings with recurrent UTI reduced symptoms of UTI and protected some patients from recurrent UTI after serial catheterizations which might reduce the need to antimicrobial therapy. In a recent veterinary study, intravesical administration of ASB *E. coli* 2-12 to dogs with recurrent UTI resulted in complete or nearly complete clinical cures in 4/9 dogs and 3 dogs also had microbiological cures at two weeks. Three of these four dogs had ASB *E. coli* 2-12 isolated from their urine at day 14.

Preventative antibiotic therapy used to be recommended, but newer information suggests that this approach may only reduce UTIs on the short-term and contributes to emergence of more resistant strains of bacteria and more resistant UTIs in the long-term. Therefore, antibiotics should not be used for prevention of UTI. Pulse antibiotic therapy for 3-5 days every few weeks is also **not** an effective strategy for management of recurrent UTI. These misuses of antibiotics are likely to induce multiple drug resistance in the organisms causing the UTI and limit the number of effective antibiotic options available for treatment of future recurrent infections.

**Subclinical bacteriuria (SBU): To treat or not to treat?**

In humans with asymptomatic bacteriuria, treatment with antimicrobials is not always administered because of the potential adverse effects of the drugs, as well as concern for emerging antimicrobial resistance. Although prospective studies regarding this issue in cats and dogs is very limited, SBU in dogs and cats may not always require treatment. One firm recommendation is to treat animals with SBU prior to and during urologic procedures (surgical or minimally invasive procedures) to minimize the risk of urosepsis. *Enterococcus* is one of the most commonly isolated organisms from dogs and cats with SBU. Treatment of this SBU often fails to resolve the SBU and selects for
greater resistance. Therefore, treatment of urine cultures positive for *Enterococcus* in animals considered to have SBU is not recommended.

**References**


