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## UROLOGY

# Urinary Tract Infections in Dogs

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Urinary tract infections (UTIs) are common in small animals, developing in up to 27% of dogs.<sup>1</sup> Nearly all infections are caused by pathogenic bacteria, although some are caused by fungi or viruses, albeit rarely. Most bacterial lower UTIs result from bacteria ascending the external genitalia and urethra. Less commonly, bacteria travel through the bloodstream and colonize the urinary tract.

Numerous innate defense mechanisms help prevent UTIs. Complete and regular voiding, along with the intrinsic properties of urine (high osmolality, antimicrobial solutes), help create a urinary tract environment that is hostile for microbes. Anatomic barriers and mucosal defenses further prevent adherence of virulent bacteria to the urothelium.

However, when these defenses are inadequate, pathogenic bacteria increase the permeability of the urothelium, allowing for passage of inflammatory solutes into the subepithelium as well as secretion of inflammatory cytokines.<sup>2</sup> The result is inflammation and pain, which are

exhibited as dysuria, pollakiuria, stranguria, and/or hematuria.

Elimination of the virulent organism can enable restoration of the normal permeability and integrity of the urothelium. Successful antimicrobial therapy requires an appropriate choice of antibiotic, including dose, frequency, and duration.

## UTI DIAGNOSIS AND LOCALIZATION

The gold standard for UTI diagnosis is urine culture. Ideally, all patients with a suspected UTI should have a urine sample collected via cystocentesis and evaluated by aerobic culture and antibiotic susceptibility testing. The techniques used to determine antibiotic susceptibility are disk diffusion and serial antibiotic dilution. The preferred method is serial antimicrobial dilution, which provides the minimum inhibitory concentration (MIC) of the antibiotic, whereas disk diffusion is considered less reliable and does not provide MICs.

### **PAINFUL CONDITION**

Signs of a urinary tract infection in dogs include lethargy, loss of appetite, increased frequency of urination, and straining at urination.

**BOX 1 Causes of Recurrent UTI****Functional or structural abnormalities**

- Urinary or fecal incontinence
- Recessed vulva
- Incomplete bladder emptying
- Vaginal or vestibular urine pooling

**Internal nidus where bacteria colonize, preventing complete elimination of infection**

- Neoplasia (benign or malignant)
- Uroliths
- Foreign material

**Altered immune function**

- Hyperadrenocorticism
- Diabetes mellitus
- Systemic or local neoplasia
- Receipt of immunosuppressive drugs or chemotherapy

**Ineffective antibiotic therapy**

- Pharmacokinetic and pharmacodynamic reasons
- Ineffective drug regimen
- Inadequate administration compliance

Efforts should be made to identify where the UTI is located within the urinary tract.<sup>3,4</sup> Although locations may overlap, UTIs can occur within the bladder (bacterial cystitis or lower UTI), kidney (pyelonephritis), and/or prostate (prostatitis). Localization is not always straightforward and is best achieved by evaluating the clinical history, presenting signs, physical examination findings, and laboratory and imaging results.

## Bacterial Cystitis

The most common signs of bacterial cystitis include dysuria, hematuria, pollakiuria, and stranguria. Clients may recognize blood in voided samples. For some dogs with underlying urinary incontinence, the magnitude of leaking may worsen when an infection is present. Urinalysis typically reveals bacteriuria, hematuria, and pyuria.

## Pyelonephritis

Pyelonephritis classically causes fever, lethargy, vomiting, and abdominal pain; however, some patients may experience few or none of these signs and

symptoms.<sup>5</sup> Blood chemistry analysis may reveal new or worsened azotemia, with glucosuria and cylindruria (casts). Urinalysis typically shows evidence of a UTI but could show inactive sediment (few red or white blood cells) in patients with an infected and obstructed kidney (pyonephrosis). Abdominal ultrasonography is not very sensitive or specific for identifying pyelonephritis; however, for some patients, it may reveal enlarged hyperechoic kidneys with perirenal effusion and echogenic debris within the renal pelves. Pyelectasia and proximal ureteral dilation are observed in patients with both pyelonephritis and ureteral obstruction. Dogs with pyelonephritis are more likely than dogs with a sterile nephroureteral obstruction to be febrile, leukopenic, and thrombocytopenic or to have leukocytosis.

## Prostatitis

Prostatitis should be suspected in male dogs, particularly intact dogs, with stranguria.<sup>6</sup> Prostatitis in castrated male dogs is rare; such dogs often have a history of recent castration. Signs and symptoms of prostatitis vary, depending on the chronicity of the infection. Acute infection is accompanied by more serious, painful clinical signs; chronic infection is often subclinical. Clinical signs relate to pain, which can be exhibited as back or abdominal pain, stiff gait, or depression. Physical examination may reveal an enlarged and asymmetric prostate, painful to palpation. Ultrasonography can show the prostate to be enlarged, heterogeneous, and possibly containing echogenic cysts.

## CLASSIFICATION OF UTIs

The 2019 International Society for Companion Animal Infectious Diseases revised the classifications of UTI.<sup>7</sup> They no longer recommend use of the terms “simple or uncomplicated” and “complicated” UTI. The revised classification has 3 diagnoses: subclinical bacteriuria, sporadic cystitis, and recurrent UTI.

## Subclinical Bacteriuria

Although not actually a UTI, the term “subclinical bacteriuria” is used for patients with bacteria identified on urine culture but no lower urinary tract signs. Older literature has often referred to “occult UTIs,” which were most likely subclinical bacteriuria. The term “occult UTI” is outdated and should no longer be used to label bacteriuria in an asymptomatic patient. Most patients with subclinical bacteriuria require no

treatment and should be considered to have colonization but not necessarily infection of the urinary tract.

## Sporadic Cystitis

Previously known as “simple” or “uncomplicated” UTI, sporadic bacterial infection causes cystitis and lower urinary tract signs. The term “complicated” UTI is no longer recommended. Bacterial cystitis may develop in patients with functional or anatomic abnormalities of the urinary tract; the presence of these abnormalities does not necessitate prolonged antibiotic therapy unless pyelonephritis or prostatitis is present.

## Recurrent UTI

A UTI is considered recurrent if the patient experiences 3 or more infections within 12 months. This condition requires investigation to determine whether it is a reinfection or a relapsing or refractory infection.

**Reinfection** is the return of a UTI—but caused by a different organism—within 6 months of discontinuation of antibiotic therapy. A **relapsing** UTI is diagnosed when the same organism is cultured again within 6 months of discontinuation of antibiotic therapy. This finding suggests that the patient has a condition that allows for recolonization or prevents total elimination of infection (**BOX 1**); for these patients, additional diagnostics are warranted. A **refractory** UTI is diagnosed when a positive urine culture is obtained while the patient is receiving appropriate antibiotic therapy (based on in vitro susceptibility testing). The possible causes for refractory UTI include the following:

- Decreased renal drug elimination (results in lower than expected urine drug concentration)
- Low drug bioavailability (e.g., due to drug compounding or gastrointestinal disease)
- Inappropriate drug dose or administration schedule
- Poor drug administration compliance

In addition, some drugs may show efficacy in vitro, but, for unknown reasons, the same effect is not present in vivo.

## TREATMENT RECOMMENDATIONS

### Subclinical Bacteriuria—To Treat or Not To Treat?

The limited studies performed in veterinary medicine

have not shown that subclinical bacteriuria results in complications.<sup>8</sup> However, human medicine has shown that more complications may arise when this condition (called asymptomatic bacteriuria in humans) is treated with antibiotics than when it is not. For veterinary patients with subclinical bacteriuria, no therapy is recommended. Neither the presence of antibiotic or multidrug resistance nor pyuria should prompt therapy. The number of bacteria obtained on culture (CFU [colony-forming unit] count) and the presence of pyuria and hematuria cannot be used to differentiate subclinical bacteriuria from cystitis. Patients with systemic disease (e.g., chronic kidney disease, diabetes mellitus, hyperadrenocorticism) do not require drug therapy unless they have clinical signs suggestive of UTI. To help prevent struvite stone formation, antibiotic therapy may be considered for patients with subclinical bacteriuria caused by urease-producing bacteria (e.g., *Staphylococcus*, *Pseudomonas*, *Proteus*).

## Sporadic Cystitis

Recommended drugs for sporadic cystitis, unless urine culture shows resistance, are amoxicillin and trimethoprim-sulfamethoxazole.<sup>7</sup> The recommended duration of therapy is 3 to 5 days (**BOX 2**). Although empiric treatment is often successful for patients with a sporadic UTI, repeated treatment without culture and susceptibility results may lead to incorrect choice of antimicrobial drug, unnecessary adverse effects, and potential selection of resistant bacteria. Clinical signs should improve within 48 hours of antimicrobial therapy initiation. If signs fail to improve, consider another cause of lower urinary tract signs (e.g., urolithiasis, neoplasia) or a resistant organism.

A UTI is considered recurrent if the patient experiences 3 or more infections within 12 months. This condition requires investigation to determine whether it is a reinfection or a relapsing or refractory infection.

**BOX 2 Empiric Antibiotics and Treatment Durations for UTIs****Sporadic Cystitis (3–5 days)**

- Amoxicillin
- Trimethoprim-sulfamethoxazole

**Prostatitis (4–6 weeks)**

- Fluoroquinolone
- Trimethoprim-sulfamethoxazole
- Clindamycin (for Gram+ bacteria only)

**Pyelonephritis (2 weeks)**

- Fluoroquinolone
- 3<sup>rd</sup>-generation cephalosporin
  - IV: cefotaxime, ceftazidime
- PO: cefpodoxime

## Prostatitis, Pyelonephritis, and Recurrent UTI

Management of these conditions is often unsuccessful unless therapy is guided by culture and susceptibility results. While culture and susceptibility results are awaited, empiric therapy should be instituted (**BOX 2**).

For patients with prostatitis, the antibiotic must achieve a high enough concentration in the prostatic tissue to cure the infection. Many antibiotics may be inefficient for treating prostatitis because most are not capable of crossing the blood–prostate barrier. Patients with prostatitis should be given a fluoroquinolone until culture results are available. The recommended durations of therapy are 4 to 6 weeks for prostatitis and 2 weeks for pyelonephritis.

Patients with recurrent UTIs often require a wide diagnostic evaluation to determine the cause. Evaluation typically includes urinary tract imaging (radiography and ultrasonography, possible computed tomography or contrast imaging), cystoscopy, urinary bladder wall biopsy and culture, endocrine testing, and more. Diagnostics should be selected individually and be based on the most likely risk factors.

Patients with reinfection (or even subclinical bacteriuria) should be evaluated for predisposing risk factors, such as urinary incontinence, anatomic abnormalities (e.g., hooded or recessed vulva), systemic immunosuppression, or endocrinopathies.<sup>7</sup>

Further efforts should be devoted to identifying the cause of prostatitis, pyelonephritis, or recurrent cystitis. Such investigation is not needed for patients with underlying anatomic abnormalities or systemic diseases that result in subclinical bacteriuria. Relapsing infection caused by the same organism is often the result of incomplete microbial elimination. Look for any nidus that could allow bacteria to evade host defenses and antimicrobial drugs (e.g., urogenital neoplasia, urolithiasis, vaginal pooling, or foreign material such as suture, stents, or cystostomy/nephrostomy tubing). In the absence of such nidus, ineffective antibiotic therapy should also be considered as a cause for microbial and clinical cure failure. For treatment of recurrent UTIs, antibiotic therapy should be guided by urine culture susceptibility results. However, persistent infection can also result from an inappropriate drug dose or administration schedule or from poor client compliance in terms of administering therapy. Altered drug metabolism or excretion (e.g., decreased glomerular filtration rate [GFR]) can also lead to subtherapeutic drug concentrations. Although rare, bacteria may be susceptible to an antibiotic in vitro but not in vivo because of the presence of biofilm or other means of evading antibiotics.

## URINARY CATHETERS

Indwelling urinary catheters are often needed for the management of urethral obstruction, trauma, acute kidney injury, and other diseases. When possible, intermittent catheterization to empty the urinary bladder is preferred to placement of an indwelling catheter because it reduces the opportunity for biofilm formation and acquisition of a UTI. However, some patients, such as cats with urethral obstruction, are better managed with an indwelling catheter to avoid repeated urethral trauma during catheterization. Urethral catheters increase the risk for bacteriuria, which develops in 10% to 55% of animals after catheterization. Aseptic catheter placement and proper catheter care can help reduce this risk (**BOX 3**). Routine monitoring of urine cytology is not recommended for patients with a urethral catheter in place. Although catheters are irritating and often cause pyuria and hematuria, these factors should not be considered justification for initiating antibiotic therapy. Prophylactic antibiotics should not be used to prevent ascending UTI in patients with indwelling or intermittent catheterization. This practice does not prevent ascending infection; rather, it selects for bacteria resistant to the administered antibiotics.

Routine culture of urine or the urethral catheter tip is not recommended.

If lower urinary tract signs (e.g., pollakiuria, stranguria, change of urine color or turbidity) develop while a catheter is in place, consider sterile cystitis or ascending bacterial cystitis as the cause. If the catheter is no longer needed for clinical management, remove it aseptically. Sterile cystitis can be treated with analgesics and nonsteroidal anti-inflammatory drugs (if not contraindicated) and allowed 1 to 3 days for clinical signs to improve.

If signs of pyelonephritis (e.g., fever, leukocytosis or leukopenia, progressive azotemia) develop in a catheterized patient, obtain a sterile urine sample. When pyelonephritis is strongly suspected, initiate empiric antibiotics while awaiting culture results.

To diagnose bacterial UTI after catheterization, the urinary catheter should be removed, and ideally, the patient should be allowed to void its bladder several times to help eliminate residual biofilm. A urine sample should be obtained via cystocentesis for urinalysis and culture. Do not culture urine from the collection bag or the catheter itself. If urethral catheterization is still needed, obtain a urine sample for urinalysis and culture via cystocentesis after removal of the previous catheter, and then aseptically place a new catheter.

Patients who lack lower urinary tract signs or symptoms at the time of urethral catheter removal do not require any specific diagnostics or therapies.

## MULTIDRUG-RESISTANT INFECTIONS

The degree of antibiotic susceptibility of UTI bacteria can vary. The general recommendation is to use an antibiotic to which the bacteria are highly susceptible. Susceptibility is suggested on urine culture MIC reports. The antibiotic breakpoint concentration (the dilution at which bacteria begin to show resistance) is designated as “<X µg/mL.” Because each antibiotic attains a different urine concentration, the “X” number cannot be compared between antibiotics (i.e., an antibiotic with a susceptibility breakpoint of <2 µg/mL should not be considered more potent than another antibiotic with a breakpoint of <8 µg/mL).

Some bacteria may be resistant to a class or even several classes of antibiotics. The urine culture susceptibility

report must be used to find the appropriate class of antibiotic that may effectively treat the infection. The “weakest” and “safest” antibiotic should be selected; antibiotics are not objectively categorized according to these qualities. Weaker classes of drugs include noncombination drugs (i.e., amoxicillin should be used before amoxicillin/clavulanic acid) and earlier generations (cefalexin [first generation] should be used before cefovecin [third generation]). Safer antibiotics are drugs with a wide margin of tolerance and low risk for systemic effects; risk for adverse effects is lower for amoxicillin than for gentamicin. Remember that these classifications are broad, and consider individual patient drug tolerance and hypersensitivity in the decision to prescribe antibiotics. For patients who are co-infected with 2 or more bacterial species, a single antibiotic may be effective if both isolates are susceptible; however, use of 2 antibiotics may be necessary.

Eliminating all infections, particularly those with intermediate susceptibility, requires ensuring adequate drug concentration at the site of infection. For patients with pyelonephritis or prostatitis, treatment effectiveness can be evaluated by tissue concentration of

### BOX 3 Indwelling Urinary Catheter Guidelines

- Always place catheters aseptically.
  - Wear sterile gloves and mask.
  - Ensure that the area is clipped, scrubbed, and draped before placing the catheter.
- Always use a closed collection system. Never leave a urethral catheter open to drain.
- Perform catheter maintenance q8h.
  - Wearing exam gloves, wipe away any visible exudate from the exterior of the urinary catheter and collection system with chlorhexidine surgical scrub and sterile water.
  - Flush the vulva or prepuce 5 times with 0.05% chlorhexidine solution.
  - Wipe the exposed catheter surface with 0.05% chlorhexidine solution.
- Do not schedule routine catheter replacements (not necessary).
- Leave catheter in place for the shortest duration possible.



The general recommendation is to use an antibiotic to which the bacteria are highly susceptible. Susceptibility is suggested on urine culture MIC reports.

antibiotics, whereas for those with bacterial cystitis, urine concentration of antibiotic can be considered.

### URINE DRUG CONCENTRATION

Many antibiotics are excreted primarily in the urine, at concentrations substantially higher than those in plasma. The urine drug concentration should be evaluated with respect to the isolate's MIC to determine the likelihood of organism elimination. Several veterinary textbooks list observed urine concentration of antibiotics at the specified dosages in healthy animals.

Urine antibiotic concentrations in veterinary patients with kidney disease have yet to be investigated. Reduced GFR may decrease drug excretion into the urine, resulting in decreased urine concentrations. Decreased urine excretion due to diminished GFR can result in plasma drug concentrations exceeding those normally observed and may cause adverse effects, especially for drugs that are substantially eliminated by the kidneys. Excretion of drugs mostly eliminated by the liver may be minimally altered in patients with decreased GFR. However, the accumulated uremic toxins and hypoproteinemia in many patients with kidney disease can lead to altered drug protein binding and abnormal drug pharmacokinetics and pharmacodynamics. Consultation with a veterinary specialist may be needed to help create a safe and effective antibiotic prescription for patients with decreased GFR.

For patients with polyuria, urine drug concentrations may be reduced because of the increased daily volume of urine and subsequent dilution of filtered antibiotic.

### MONITORING RESPONSE TO THERAPY

Patients with sporadic cystitis may not require rigorous monitoring. However, patients with prostatitis, pyelonephritis, or recurrent infections should be monitored very closely. Recurrent cystitis does not necessarily require a prolonged course of antibiotic therapy. The following protocol is recommended for monitoring response to therapy in patients with recurrent UTI.<sup>9</sup>

- **Reculture urine after 5 to 7 days of antibiotic therapy.** Doing so confirms that the prescribed dose and frequency of the drug were successful in treating the isolated organism. This culture also may reveal an additional isolate that was not identified on the initial culture. Observation of any bacterial growth at this time suggests treatment failure; reconsider the choice of antibiotic and dosage and administration frequency.
- **Reculture urine 3 days before discontinuing antibiotic therapy.** This step is optional, but it confirms that when therapy was discontinued the culture was still negative. Positive bacterial growth at this stage suggests a refractory infection or newly inoculated organism. Patients with a positive culture should be investigated for any nidus of infection (e.g., urolithiasis, anatomic abnormality, local neoplasia), and treatment should be altered and new therapy instituted for the same duration as previously intended.
- **Reculture urine 7 to 14 days after discontinuing antibiotic therapy.** Positive growth should prompt investigation for causes of relapse or reinfection.

Recurrent UTIs may be challenging to cure. However, understanding drug pharmacokinetics and pharmacodynamics and potential alterations in the animal's metabolism/excretion of the drug can help increase the likelihood of treatment success.

### NONTRADITIONAL THERAPIES

Various supplements and holistic therapies that have been given to patients with UTIs include cranberry extract, D-mannose, glycosaminoglycans, and other herbal remedies. Unfortunately, most have not been formally evaluated against a placebo. Most of those that have been evaluated have proven to be ineffective for preventing or treating UTI.<sup>10</sup> Future studies may optimize dosing and lead to better outcomes; however, no current evidence supports use of such therapies in the management of UTI.

## SUMMARY

Localizing and classifying a UTI will help determine the best treatment. Most UTIs are successfully treated with commonly used drugs, dosages, and administration intervals. However, treatment can be challenging when the infection involves the kidneys and/or prostate. In addition, creating an appropriate antibiotic prescription for patients with kidney disease can be difficult because of reduced drug clearance. Proper understanding of the location of the UTI along with drug pharmacology can allow for successful treatment of these challenging infections. **TVP**

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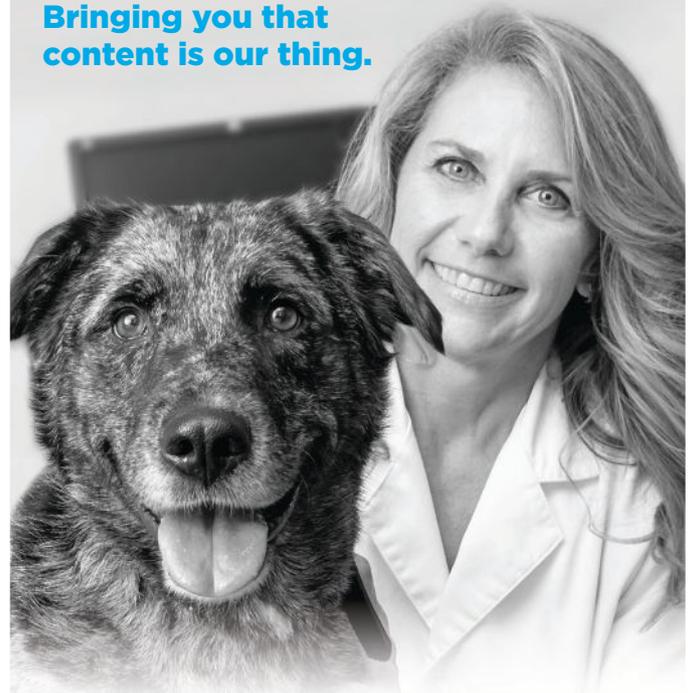
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## CONTINUING EDUCATION

# Urinary Tract Infections in Dogs

## TOPIC OVERVIEW

Urinary tract infections (UTIs) are common in small animal practice; it has been reported that up to 27% of dogs will develop infection at some time in their lives. Proper understanding of the location of the UTI along with drug pharmacology can allow for successful treatment of these challenging infections.

## LEARNING OBJECTIVES

The reader will learn how to diagnose, treat, and manage urinary tract infections (UTIs) in their canine patients. They will gain an understanding of how localizing and classifying UTI will help to determine the best treatment of these challenging infections. They will learn about commonly used drugs, including proper dosages and administration intervals. They will be able to develop a treatment strategy when the infection involves the kidneys and/or prostate.

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- A urinary tract infection in a castrated male dog with stranguria, pollakiuria, fever, and leukocytosis would probably be localized to**
  - Bacterial cystitis
  - Subclinical bacteriuria
  - Pyelonephritis
  - Prostatitis
- Appropriate therapy for bacterial prostatitis may include all of the following EXCEPT**
  - Enrofloxacin
  - Amoxicillin/clavulanic acid
  - Clindamycin
  - Trimethoprim-sulfamethoxazole
- Antibiotics for sporadic cystitis should be given for**
  - 3-5 days
  - 7-10 days
  - 10-14 days
  - 4-6 weeks
- Subclinical bacteriuria should be empirically treated with which antibiotic?**
  - Amoxicillin
  - Cephalosporin
  - Trimethoprim-sulfamethoxazole
  - No antibiotic needed
- The best method for diagnosing a catheter-related urinary tract infection is**
  - Obtain urine via cystocentesis after the urinary catheter has been removed
  - Remove the urinary catheter and culture the tip
  - Submit urine from the closed collection system for culture
  - No diagnostics needed; therapy can be based on clinical signs
- Compared with placebo, cranberry extract has been shown to prevent canine urinary tract infection.**

True  
False
- All of the following are necessary for proper placement and maintenance of a urinary catheter EXCEPT**
  - Prophylactic antibiotic administration
  - Aseptic patient preparation (e.g., clipping, surgical scrub, draping)
  - Closed collection system
  - Routine catheter cleaning
- Patients with hyperadrenocorticism and bacteriuria should always be considered to have a complicated urinary tract infection.**

True  
False
- Which of these antibiotics would be appropriate empiric therapy for sporadic cystitis?**
  - Amoxicillin/clavulanic acid
  - Cefpodoxime
  - Marbofloxacin
  - Trimethoprim-sulfamethoxazole
- Recurrent urinary tract infections may result from the presence of all of the following EXCEPT**
  - Functional or structural urinary tract abnormalities
  - Abnormal structure within urinary tract (e.g., urolith, neoplasia)
  - Altered immune function
  - Multidrug-resistant bacteria