# *Seven Habits for the Highly Effective Treatment of Urinary Tract Infections*

*Joseph W. Bartges, DVM, PhD, DACVIM, DACVN*

Table of Contents

**Managing Microbes™ Proceedings**

*Industry Neutrality Review*

Content Donated By Pfizer

- Introduction
- 2004
- **2007**
  - Compliance: What It Is Does
  - Seven Habits for Urinary Treatment
  - Antimicrobial Therapy in Cats
  - Recurrent Skin Infections

A urinary tract infection (UTI) occurs when a breach (either temporary or permanent) in host defense mechanisms occurs and a virulent microbe in sufficient numbers is allowed to adhere, multiply and persist in a portion of the urinary tract. These infections typically involve bacteria; however, they can be caused by fungi and viruses. Infection may predominate at a single site, such as the kidney (pyelonephritis), ureter (ureteritis), bladder (cystitis), urethra (urethritis), prostate (prostatitis), vagina (vaginitis), or at two or more of these sites. Because a UTI may involve more than one location, it may be more relevant to identify the infection anatomically--that is, upper urinary tract (kidneys and ureters) versus lower urinary tract (bladder, urethra, and prostate or vagina). The infection may or may not produce clinical signs. The pathogenesis of UTI represents a balance between uropathogenic infectious agents and host resistance. Urinary tract infections are treated with antimicrobial agents; however, the status of host defense mechanisms is important in development of a UTI and in successful treatment and prevention.

Bacterial UTI is estimated to occur in 14% of all dogs during their lifetime.[1] It is more common in female dogs than in males[2-5] and more common in cats older than 10 years of age than in younger cats; the incidence of bacterial UTI increases with age.[6-8]

## 1. Diagnose the Problem

A bacterial UTI is only one cause of hematuria, pyuria, and clinical signs of lower urinary tract disease. Appropriate treatment is dependent on the correct diagnosis.

### Historical Information and Physical Examination Findings

Dogs and cats with UTI may or may not have clinical signs. Signs vary and depend on the interaction of the following factors: 1) virulence and numbers of the uropathogen, 2) presence or absence of predisposing causes, 3) the body's compensatory response to infection, 4) the duration of infection, and 5) the site of infection (**Table 1**). Pollakiuria, stranguria, dysuria, and inappropriate urination may be observed with lower UTIs. Animals with upper UTIs may exhibit pain localized to one or both kidneys, hematuria, septicemia, or renal failure (with resultant clinical signs if both kidneys are infected). If UTI is associated with a predisposing condition, such as diabetes mellitus, hyperadrenocorticism, or bladder neoplasia, then clinical signs associated with the predisposing condition are also often present. Female dogs with abnormalities of the vulva (**Figure 1**), perivulvar dermatitis, or vaginal stenosis (**Figure 2**) may beat increased risk for UTI.[9] Male cats with perineal urethrostomies are also at increased risk for UTI.[10]

Some animals may have infection of both the upper and lower urinary tracts, especially if renal failure is present.

**Table 1. Abnormalities That Help to Localize Urinary Tract Infections**

| Sites of Urinary Tract Infection | History | Physical Examination | Laboratory Findings | Imaging Studies |
|---|---|---|---|---|
| **Lower urinary tract** | Dysuria, pollakiuria<br>Urge incontinence<br>Signs of abnormal detrusor reflex (overflow incontinence, large residual volume)<br>Gross hematuria at end of micturition<br>Cloudy urine with abnormal odor<br>No systemic signs<br>Recent catheterization or urethrostomy | Small, painful thickened bladder<br>Palpable masses in urethra or bladder<br>Flaccid bladder wall, large residual volume<br>Abnormal micturition reflex<br>± Palpation of uroliths | CBC = normal<br>Urinalysis = pyuria, hematuria, proteinuria, bacteriuria<br>Urine culture - significant bacteriuria | Normal kidneys<br>Structural abnormalities of lower urinary tract<br>± Urocystoliths and/or urethroliths<br>± Thickening of bladder wall and irregularity of mucosa<br>Rarely intraluminal gas formation (emphysematous cystitis) |
| **Upper urinary tract** | Polyuria, polydipsia<br>± Signs of systemic infection<br>± Renal failure | ± No detectable abnormalities<br>± Fever and other signs of systemic infection<br>Kidneys normal or increased in size<br>± Abnormal (renal) pain | CBC = ± leukocytosis<br>Urinalysis = pyuria, hematuria, proteinuria, bacteriuria, white blood cells or granular casts<br>Impaired urine concentration<br>± Azotemia and other findings of renal failure | Renomegaly<br>± Abnormal kidney shape<br>± Nephroliths, ureteroliths<br>± Dilated renal pelves, dilated pelvic diverticula<br>± Evidence of outflow obstruction |

| | | | | |
|---|---|---|---|---|
| **Acute prostatitis or prostate abscess** | Urethral discharge independent of micturition<br>Signs of systemic infection<br>± Reluctance to urinate or defecate | ± Fever and other signs of systemic infection<br>± Painful prostate and/or painful abdomen<br>± Prostatomegaly or asymmetric prostate | CBC = ± leukocytosis<br>Urinalysis = pyuria, hematuria, proteinuria, bacteriuria<br>Cytology of prostate = inflammation and infection | ± Indistinct cranial border of prostate<br>± Prostatomegaly<br>± Prostatic cyst<br>± Reflux of contract medium into prostate |
| **Chronic prostatitis** | Recurrent UTI<br>Urethaal discharge independent of urination<br>± Dysuria | Often no detectable abnormalities<br>± Prostatomegaly or asymmetric prostate | CBC = normal<br>Urinalysis = pyuria, hematuria, proteinuria, bacteriuria | ± Prostatomegaly<br>± Prostate cysts<br>± Prostate mineralization |

CBC = complete blood count

**Figure 1.** Recessed vulva in a 4 year old, spayed female mixed-breed dog with recurrent bacterial urinary tract infections.

**Figure 2.** Vaginal stricture in a 1 year old, spayed female mixed-breed dog with urinary incontinence and recurrent bacterial urinary tract infections.

### Urinalysis

Urinalysis should be a routine part of a minimum database. A complete urinalysis involves determining urine specific gravity (USG) using a refractometer, chemical analysis using analytical test pads on dipsticks, and sediment examination. Collection of urine by cystocentesis is the best way to evaluate a patient for UTI. If infectious prostatitis or vaginitis is suspected, then those conditions are evaluated using different techniques.

With UTI, USG varies depending on whether the infection involves the upper urinary tract or an associated disease is present. Dipstick analysis often, but not always, reveals hematuria and proteinuria. Leukocyte esterase (white blood cells) and nitrite (bacteria) test pads are not reliable in dogs and cats and should not be used.[9]

Examination of urine sediments should be a routine part of a complete urinalysis. Significant numbers of white blood cells (>0 to 5 per high-power field) associated with hematuria and proteinuria in a properly collected urine sample suggest inflammation. Detection of significant microburia with

pyuria indicates active inflammation associated with an infection. Bacteria and fungi may be difficult to identify in dilute urine, making a diagnosis of UTI problematic. Urinary tract infection, especially a bacterial UTI, may also be present without concurrent inflammation if host defenses are compromised (e.g., hyperadrenocorticism or FeLV).[7,10-15]

Rod-shaped bacteria may be identified in unstained preparations of urine sediment if more than 10,000 bacteria/mL are present, but may not be consistently detected if they are present in fewer numbers. Cocci are difficult to detect in urine sediment when there are fewer than 100,000 bacteria/mL.[16] Although detection of bacteria on urine sediment examination suggests bacterial UTI, it should be verified by urine culture. Urine sediment may be stained with Wright's stain (**Figure 3**), Gram's stain, or new methylene blue to aid in detection of microbes; however, urine culture is the "gold standard" for confirmation of UTI. Failure to detect bacteria on examination of urine sediment does not exclude their presence or rule out UTI.

**Figure 3.** Photomicrograph of a urine sediment stained with a modified Wright's stain showing neutrophils, red blood cells, and rod-shaped bacteria (*Escherichia coli*) from a dog with a bacterial urinary tract infection (original magnification 400X).

## 2. Culture of Urine

### Urine Collection

Urine should be collected by cystocentesis for culture. With lower urinary tract disease, it can be difficult to collect a sample by this method; therefore, it may be necessary to collect urine for culture by catheterization or, less desirably, voiding. For these techniques, clean the external genitalia of the patient. Perivulvar fur may require clipping to prevent contamination. Although urinary catheterization of dogs is usually accomplished without chemical restraint, cats require sedation or anesthesia. Use a sterile catheter and collection container (syringe or collection cup with a tight-fitting lid). If results of quantitative culture of urine samples obtained by catheterization or mid-stream voiding are equivocal following after cultures, collect urine by cystocentesis.

Even low numbers of bacteria in urine collected aseptically by cystocentesis indicate UTI; however, false-positive results may occur if the hypodermic needle penetrates a loop of intestine during the procedure or if the sample is contaminated during handling. Contamination usually involves recovery of more than one organism.

### Urine Culture

Urine culture is the "gold standard" for diagnosing UTI. A diagnosis of UTI based only on clinical signs, hematuria, and/or urinary tract inflammation may be a misdiagnosis that leads to inadequate or inappropriate treatment. There are circumstances during which antimicrobial therapy is initiated without results of urine culture; however, samples for urine culture should be collected before therapy is initiated. If antimicrobial therapy has been

started, it should be discontinued for 3 to 5 days before urine culture is done to minimize inhibition of microbial growth.

A urine culture is the most definitive means of diagnosing a bacterial UTI. Care must be taken to collect, preserve, and transport the urine sample to avoid contamination or proliferation or death of bacteria.[17] Urine specimens for aerobic bacterial culture should be transported and stored in sealed, sterilized containers. Processing should begin as soon as possible. If laboratory processing is delayed by more than 30 minutes, refrigerate the specimen at 4°C. At room temperature, bacterial counts can double every 20 to 45 minutes, and multiplication or destruction of bacteria can occur within 1 hour of collection.

If urine samples cannot be processed immediately for urine culture, there are several alternatives. Blood agar and MacConkey agar plates may be inoculated and incubated for 24 hours. Use a calibrated bacteriologic loop or microliter mechanical pipette that delivers exactly 0.01 or 0.001 milliliters of urine to the culture plates. Streak the urine over the plates by conventional methods. Blood agar supports growth of most aerobic uropathogens and MacConkey agar provides information that aids in identification of bacteria and prevents "swarming" of Proteus species. Incubate the plates in an incubator or under an incandescent light.[19] (**Figure 4**). If bacterial growth occurs on the plate after 24 hours, the plate may be submitted for identification and determination of antimicrobial sensitivities, or antimicrobial susceptibility may be determined by using the agar disk diffusion method.[19,20] If no growth occurs after 24 hours, then the plates maybe discarded.

**Figure 4A.** Incubation of a blood agar microbiological plate using an incandescent light to maintain surface temperature at 38°C.

**Figure 4B.** Blood agar plate demonstrating growth of bacteria after incubation with the incandescent light.

Commercially available urine culture collection tubes containing preservative that are refrigerated after collection may be used to preserve specimens for up to 72 hours.[21]

### *Qualitative Urine Culture*

A qualitative urine culture involves isolating and identifying bacteria in urine--it does not include counting the number of bacteria. Although urine in the bladder is normally sterile, urine that passes through the distal urogenital tract often becomes contaminated with resident flora (**Table 2**).[2] Therefore, interpretation of bacteria in urine collected by catheterization or voiding is often difficult to interpret even with quantification of bacteria. For this reason, a diagnostic urine culture should include quantifying bacterial numbers in addition to identifying the organism and antimicrobial susceptibility.

**Table 2. Bacteria Detected in the Urogenital Tract of Healthy Male and Female Dogs**

| Genus | Distal Urethra Males | Prepuce | Vagina |
|---|---|---|---|
| Acinetobacter | | + | + |
| Bacteroides | | | + |
| Bacillus | | + | + |
| Citrobacter | | | + |
| Corynebacterium | + | + | + |
| Enterococcus | | | + |
| Enterobacter | | | + |
| Escherichia | + | + | + |
| Flavobacterium | + | + | + |
| Haemophilus | + | + | + |
| Klebsiella | + | + | + |
| Micrococcus | | | + |
| Moraxella | | + | + |
| Mycoplasma | + | + | + |
| Neisseria | | | + |
| Pasteurella | | + | + |
| Proteus | | + | + |
| Pseudomonas | | | + |
| Staphylococcus | + | + | + |
| Streptococcus | + | + | + |
| Ureaplasma | + | + | + |

From Bartges JW. Bacterial urinary tract infections. In: Ettinger SJ, Feldman EC, eds. *Textbook of Veterinary Internal Medicine*. 6th edition. Philadelphia, Pa: W.B. Saunders Company; 2005:1800-1808.

### *Quantitative Urine Culture*

A quantitative urine culture includes isolation and identification of the organism, and determination of the number of bacteria (colony-forming units per unit volume). Quantitation of bacteria enables interpretation of the significance of bacteria present in a urine sample. Caution should be exercised when interpreting quantitative urine cultures obtained by mid-stream voiding or manual expression. Although urine obtained from most dogs without UTI was either sterile or contained fewer than 10,000 colony-forming units (CFUs)/mL of urine (**Table 4**), counts of 100,000 or more CFUs/mL occurred often enough to make collection of urine by these methods unreliable.[22] The definition of significant bacteruria in cats involves lower numbers of organisms because cats seem to be more resistant to UTI than dogs and humans.

**Table 4. Interpretation of Quantitative Urine Cultures in Dogs and Cats*[16]**

| Method of Collection | Significant | | Suspicious | | Contaminated | |
|---|---|---|---|---|---|---|
| | Dogs | Cats | Dogs | Cats | Dogs | Cats |
| Cystocentesis | ≥ 1000 | ≥ 1000 | 100 to 1,000 | 100 to 1,000 | ≤ 100 | 100 |
| Catheterization | ≥ 10,000 | ≥ 1000 | 1000 to 10,000 | 100 to 1000 | ≤ 10,000 | ≤ 1000 |
| Mid-stream voiding | ≥ 100,000 | ≥ 10,000 | 10,000 to 90,000 | 1,000 to 10,000 | ≤ 10,000 | ≤ 1000 |
| Manual compression | ≥ 100,000 | ≥ 10,000 | 10,000 to 90,000 | 1,000 to 10,000 | ≤ 10,000 | ≤ 1000 |

*Colony-forming units/mL urine. Data represent generalities. Occasionally, bacterial UTI may be detected with fewer organisms (i.e., false-negative results)
Collecting samples mid-stream can cause contamination, and such samples can contain 10,000 or more colony-forming units/mL (i.e., false-positive results); thus, they should not be used for routine diagnostic culture.

### Antimicrobial Susceptibility Testing

Administration of antimicrobial agents is the cornerstone of UTI treatment. The agent is chosen on the basis of antimicrobial susceptibility testing. The agent selected should be easy to administer; associated with few if any side effects; inexpensive; unlikely to adversely affect the patient's intestinal flora; and able to attain tissue or urine concentrations that will exceed the minimum inhibitory concentration (MIC) for the uropathogen by at least

four-fold.[16] The MIC is the minimum concentration of an antimicrobial drug that inhibits growth of the uropathogen.

### *Agar Disk Diffusion Technique*

Antimicrobial susceptibility testing is often done by using agar disk diffusion (Kirby-Bauer),[23] which is adequate in most bacterial UTI. The agar disk diffusion method consists of Mueller-Hinton agar plates that have been inoculated with a standardized suspension of a single uropathogen. Paper disks impregnated with different antimicrobial drugs are placed on the plate. After 18 to 24 hours of inoculation at 38°C, antimicrobial susceptibility is estimated by measuring zones of inhibition of bacterial growth surrounding each disk (**Figure 5**). Zones of inhibition are then interpreted in light of established standards and recorded as resistant, susceptible, or intermediately susceptible. Because of differences in ability of various antimicrobials to diffuse through agar, the antimicrobial disk surrounded by the largest zone of inhibition is not necessarily the drug most likely to be effective. Also, because the concentration of antimicrobial (except nitrofurantoin) in the paper disks is similar to the typical serum concentration of the drug, drugs that are found to be resistant by the agar disk diffusion method may be effective in the urinary tract if they are excreted in high concentrations in urine (e.g., ampicillin and cephalexin).

**Figure 5.** Kirby-Bauer (agar gel diffusion) susceptibility test of a urine sample infected with *Escherichia coli* collected from a dog.

### *Antimicrobial Dilution Technique*

Antimicrobial dilution susceptibility tests are designed to determine the MIC. After inoculation and incubation of uropathogens into wells containing serial two-fold dilutions of antimicrobial drugs at concentrations achievable in tissues and urine, the MIC is defined as the lowest antimicrobial concentration (or highest dilution) that allows no visible bacterial growth. The MIC is several dilutions lower than the minimum bactericidal concentration of drugs. In general, the antimicrobial agent is likely to be effective if it can achieve a concentration four times that of the MIC (**Table 5**). Many antimicrobial drugs that are renally excreted reach concentrations in urine that are 10 to 100 times greater than the serum concentration.

**Table 5. Average Urine Concentrations of Some Antimicrobial Agents in Dogs***

| Drug | Daily Dose (ml/kg) | Route of Administration | Mean Urine Concentration (± sd) |
|---|---|---|---|
| Amikacin | 5 | SQ | 342 ± 143 µg/mL |
| Amoxicillin | 11 | PO | 202 ± 93 µg/mL |
| Ampicillin | 26 | PO | 309 ± 55 µg/mL |

| | | | |
|---|---|---|---|
| Cephalexin | 18 | PO | 500 µg/mL |
| Chloramphenicol | 33 | PO | 124 ± 40 µg/mL |
| Enrofloxacin | 5 | PO | 40 ± 10 µg/mL |
| Gentamicin | 2 | SQ | 107 ± 33 µg/mL |
| Hetacillin | 26 | PO | 300 ± 156 µg/mL |
| Kanamycin | 4 | SQ | 530 ± 151 µg/mL |
| Nitrofurantoin | 4.4 | PO | 100 µg/mL |
| Penicillin G | 36,700 units/kg | PO | 295 ± 211 µg/mL |
| Penicillin V | 26 | PO | 148 ± 99 µg/mL |
| Sulfisoxazole | 22 | PO | 1466 ± 832 µg/mL |
| Tetracycline | 18 | PO | 139 ± 65 µg/mL |
| Trimethoprim/ sulfadiazine | 13 | PO | 55 ± 19 µg/mL |
| Tobramycin | 2.2 | SQ | 66 ± 39 µg/mL |
| *SD = standard deviation, SQ = subcutaneous, PO = oral | | | |

### 3. Assess the Defenses

The urogenital tract communicates with the external environment. Most UTIs result from ascending migration of pathogens from the distal urogenital tract into normally sterile environments. A resident population of bacteria is usually present in the lower urogenital tract; the presence of these bacteria may decrease establishment of a uropathogen or may become a uropathogen if normal host defenses are altered (**Table 2**). Although the urinary tract communicates with the microbial-laden external environment, most of the urinary tract is usually sterile and all of it is normally resistant to infection. Mechanisms of host resistance to UTI may be divided into the following two categories: natural inherent resistance factors, and acquired or induced resistance factors that are activated after a UTI (**Table 3**). Systemic host defenses play a role in preventing hematogenous spread of pathogens to and from the urinary tract; however, local host defense mechanisms are the initial defense in preventing ascending infection[24] (**Table 3**). The host defense mechanisms also seem to differ between the upper and lower urinary tracts. For example, inducing diuresis is beneficial in preventing experimental induction of bacterial

pyelonephritis in rats[25]; however, dilute urine seems to increase an animal's susceptibility to bacterial infection of the lower urinary tract.[7,26]

**Table 3. Natural and Acquired Host Defenses of the Urinary Tract**

- Normal micturition
  - Adequate urine volume
  - Frequent voiding
  - Complete voiding
- Anatomical structures
  - Urethral high-pressure zones
  - Surface characteristics of urothelium
  - Urethral peristalsis
  - Prostatic secretions (antibacterial fraction and immunoglobulins) Length of urethra
  - Ureterovesical flap valves
  - Ureteral peristalsis
  - Glomerular mesangial cells (?)
  - Extensive renal blood supply and flow
- Mucosal defense barriers
  - Antibody production
  - Surface layer of glycosaminoglycans
  - Intrinsic mucosal antimicrobial properties
  - Exfoliation of urothelial cells
  - Bacterial interference by commensal microbes of distal urogenital tract
- Antimicrobial properties of urine
  - Extreme high and low urine pH
  - Hyperosmolality
  - High concentration of urea
  - Organic acids
  - Low-molecular-weight carbohydrates
  - Tamm-Horsfall mucoproteins
- Systemic immunocompetence
  - Cell-mediated immunity
  - Humoral-mediated immunity

From Bartges JW. Bacterial urinary tract infections. In: Ettinger SJ, Feldman EC, eds. *Textbook of Veterinary Internal Medicine*. 6th edition. Philadelphia, Pa: W.B. Saunders Company; 2005:1800-1808.

Not all microbes, particularly bacteria, are pathogenic. For example, of the more than several hundred serotypes of *Escherichia coli*, fewer than 20 account for the majority of bacterial UTIs.[27] Because *E. coli* is the most common bacterial uropathogen in humans, dogs, and cats, its virulence has been studied more extensively than that of any other uropathogen. Uropathogens typically have more than one virulence factor; therefore, the absence of one factor does not necessarily cause a loss of uropathogenicity. Likewise, bacteria that are normally nonpathogenic in a healthy patient may become pathogenic in a patient with altered host defenses.

### Evaluating Host Defenses: Laboratory, Imaging, and Endoscopy

Patients with UTI, especially commonly recurring infection, should undergo additional evaluation with the goal of identifying predisposing and, it is hoped, correctable problems. Unless septicemia or renal failure is present, results of complete blood cell counts are normal. If septicemia is present, leukocytosis with a left shift may be present. Lower UTI does not cause changes in blood values unless another disease process is present. With upper UTIs, serum biochemical analysis may be normal or may indicate renal failure (if both kidneys are diseased). If UTI is associated with another disease, then changes in laboratory parameters may reflect the associated condition. In cats, FeLV and FIV infection increases risk for UTI.[7]

In many dogs and cats with UTI, results of imaging studies are normal. Survey abdominal radiographs may show uroliths (**Figure 6**), renomegaly or small kidneys, or other defects that may predispose the patient to UTI. Some dogs may have pelvic displacement of the urinary bladder (so called "pelvic bladder") (**Figure 7**), which can be associated with urinary incontinence and UTI, although it has been noted in dogs without disease.[28] If no abnormalities are found by survey abdominal radiography, ultrasonography or contrast radiography should be performed. The upper urinary tract may be evaluated by excretory urography (**Figure 8**), whereas the lower urinary tract maybe evaluated by contrast cystourethrography, double-contrast cystography, and contrast vaginourethrography. A potential complication of performing contrast radiography of the lower urinary tract is inducing UTI. Ultrasonography is a noninvasive technique and is useful in evaluating the echo texture and architecture of the urinary tract except for the distal urethra (**Figure 9**). In humans, nuclear scintigraphy using 99Tcm-labelled dimercaptosuccinic acid may be useful for evaluating pyelonephritis, although it has not been used in dogs.[29,30]

**Figure 6.** Lateral abdominal radiograph of a 4-year-old, spayed female mixed-breed dog showing two radiodense urocystoliths (arrow). The urocystoliths comprised struvite and resulted from a bacterial urinary tract infection caused by *Staphylococcus intermedius*.

**Figure 7.** Lateral pneumocystogram from a 4-year-old, spayed female English setter. The patient had urinary incontinence demonstrating a "pelvic bladder." Note that the trigone is located in the pelvic

| | |
|---|---|
| | canal rather than in the abdomen. |
|  | **Figure 8.** Excretory urography of a 6-month-old, intact female Chow with urinary incontinence and recurrent bacterial urinary tract infections. The right ureter (U) is ectopic and dilated, and hydronephrosis of the right kidney is present. A Foley catheter (F) is placed within the urinary bladder (the balloon is inflated and located at the trigone). |
|  | **Figure 9.** Ultrasonography of the lower urinary tract of an 8-year-old, intact male Rhodesian ridgeback with abscesses (A) in the prostate. The urinary bladder is visible. |

Endoscopy of the lower urinary tract may be useful in identifying mucosal and intraluminal lesions that may predispose to UTI. In one study, a urolith not visible by survey radiography was visualized by cystoscopy in a cat.[31] Disadvantages of cystourethroscopy include the need for anesthesia, potential for trauma to the lower urogenital tract, and difficulty performing the procedure in male cats.

### 4. Uncomplicate the Complicated

Bacteria that commonly cause UTI are similar between dogs and cats. Infections caused by *E. coli* usually account for one third to one half of all organisms isolated from urine. Gram-positive cocci are the second major group of uropathogens. *Staphylococcus, Streptococcus*, and *Enterococcus* species account for one fourth to one third of recovered isolates. Bacteria causing the remaining one fourth to one third of bacterial UTI include *Proteus, Klebsiella, Pasteurella, Pseudomonas, Corynebacterium*, and *Mycoplasma* species; however, each of these types of bacteria has been found in only a few instances.[6,7,32-36]

Approximately 75% of bacterial UTI in dogs are caused by a single species of pathogen, approximately 20% are caused by two species, and approximately 5% are caused by three species.[34] A similar pattern is found in cats[7] (Bartges JW, Lucas P, Jesse L. Unpublished observation. 2003).

Uncomplicated UTIs are those in which no underlying structural, neurologic, or functional abnormality is identified. Reproductively intact dogs, all cats, and animals with identifiable predisposing causes for UTI (e.g., renal failure, hyperadrenocorticism, diabetes mellitus) should be considered to have complicated UTI. Pyelonephritis and prostatitis are examples of complicated UTI. Animals with recurrent UTI (relapses or reinfections) are also considered to have complicated UTI.

## 5. Treat the Treatable

### Uncomplicated UTI

Uncomplicated bacterial UTI can usually be treated successfully with a 10 to 14 day course of an appropriate antimicrobial agent. If the proper antimicrobial is chosen and administered at the appropriate dosage and frequency, clinical signs should resolve within 48 hours. Results of a complete urinalysis should improve within this same time frame. If possible, urine cultures should be done 5 to 7 days after cessation of antimicrobial therapy.

Uncomplicated UTI of acute onset can be treated without results of antimicrobial susceptibility testing as long as the patient has not been given antimicrobial agents within the past 4 to 6 weeks and the infection is an initial or infrequent occurrence. In this situation, the antimicrobial should be chosen for its known properties and with knowledge of bacteria that commonly cause UTI (**Table 6**). Identification of bacteria on examination of urine sediment, especially if Gram's staining has been done, increases the likelihood of empirically choosing an appropriate antimicrobial. For example, *E. coli* is the most common cause of bacterial UTI in dogs and cats and is a gram-negative rod associated with aciduria. Staphylococcus species, on the other hand, is a gram-positive coccus associated with alkaluria because it produces urease, which metabolizes urea to ammonia resulting in an alkaline urine pH.

Use of fluoroquinolones for empirical treatment of bacterial UTI is discouraged because many gram-positive organisms are inherently resistant and many gram-negative organisms, especially *E. coli*, are becoming resistant to this class ofantimicrobials.[37,38]

**Table 6. Estimate of Susceptibility of Uropathogens to Common Antimicrobial Agents**

| Uropathogen | Drugs of Choice | Alternatives |
|---|---|---|
| *Enterobacter* species | Trimethoprim-sulfadiazine | Cephalosporins (first- and second-generation), gentamicin, nitrofurantoin |
| *Escherichia coli** | Trimethoprim-sulfadiazine | Cephalosporins (first- and second-generation), fluoroquinolones, gentamicin |
| *Klebsiella* species* | Cephalosporins (first-generation) | Amikacin, gentamicin, trimethoprim-sulfadiazine, cephalosporins (second- and third-generation) |

| | | |
|---|---|---|
| *Mycoplasma**, *Ureaplasma* | Fluoroquinolones | Tetracyclines |
| *Proteus* species* | Amoxicillin, ampicillin, amoxicillin-clavulanate | Cephalosporins (first- and second-generation), gentamicin, nitrofurantoin, trimethoprim-sulfadiazine |
| *Pseudomonas aeruginosa** | Fluoroquinolones | Tetracyclines, gentamicin, cephalosporins (first, - second, - and third-generation) |
| *Staphylococcus* species* | Amoxicillin, ampicillin, amoxicillin-clavulanate | Cephalosporins (first-generation), nitrofurantoin, trimethoprim-sulfadiazine |
| *Streptococcus* species, *Enterococcus* species | Amoxicillin, ampicillin, Amoxicillin, ampicillin, | Cephalosporins (first-generation), nitrofurantoin, trimethoprim-sulfadiazine |
| *Prior treatment with antimicrobial agents may alter susceptibility of uropathogens to these drugs. | | |

**Complicated UTI**

Treatment with antimicrobials for longer than the routine 10 to 14 days may be indicated and is usually continued for 4 to 6 weeks. Urine should be evaluated in the first week of treatment for response to therapy and before therapy is discontinued. After antimicrobial therapy is completed, prophylactic antibiotic treatment may be necessary to control bacterial UTIs that are difficult to eradicate or recur frequently.

**Recurrent UTI**

***Relapse***

Relapse is defined as recurrence of a UTI due to the same organism. Relapses usually occur days to weeks after discontinuation of antimicrobial therapy. Possible causes of relapse include use of an inappropriate antimicrobial agent; administering an appropriate antimicrobial agent at the inappropriate dosage, frequency, or duration; or complicating factors. A urine culture should be evaluated before antimicrobial therapy is restarted. Further diagnostic evaluation for predisposing causes is also indicated.

***Reinfection***

Reinfection is defined as infection with an organism different from that which caused the original infection. Reinfection usually occurs sometime after cessation of antimicrobial therapy. Although predisposing risk factors may be present, many animals that become reinfected often do not have identifiable risk factors. If reinfections are infrequent, each episode may be treated as an uncomplicated UTI. However, if reinfections occur more than three times per year, then animals should be treated as having a

complicated UTI. Prophylactic antimicrobial therapy may also be indicated.

### *Superinfection*

Superinfection occurs when a second bacterial organism is isolated while an animal is receiving antimicrobial therapy. This organism often has a high degree of antibiotic resistance. A UTI that occurs in animals receiving antimicrobial therapy that also have an indwelling urethral catheter is an example of a superinfection.[39]

## 6. Prevent the Preventable

### Prophylactic Antimicrobial Therapy

There are no good studies evaluating prophylactic antimicrobial therapy in animals with frequent reinfections. Before prophylactic therapy is done, urine culture and susceptibility testing should be conducted to ensure that the bacterial UTI has been eradicated. Select a drug that is excreted in high concentrations in urine and unlikely to cause adverse effects. Often a fluoroquinolone, cephalosporin, or betalactam antimicrobial is chosen. Give the antimicrobial at approximately one third the therapeutic daily dose immediately after the patient has voided and when the drug and its metabolites will be retained in the urinary tract for 6 to 8 hours. This is typically done at night. Another technique involves giving therapeutic dosages of an antimicrobial agent for 1 week out of 4. As mentioned, select a drug that achieves high concentration in urine and is unlikely to cause adverse effects. With either method, give the drug for a minimum of 6 months. Collect urine samples, preferably by cystocentesis (not by catheterization as this causes bacterial UTI), every 4 to 8 weeks for urinalysis and quantitative urine culture. If there is no bacterial UTI, then continue with prophylactic therapy. If a bacterial UTI is identified, treat the active (break-through) infection as a complicated bacterial UTI. If a breakthrough bacterial UTI does not occur after 6 months of prophylactic antimicrobial therapy, therapy may be discontinued and the patient should be monitored for reinfection.[40,41]

### Methenamine

Methenamine is not related to other antimicrobial agents. It is available either as a salt with mandelic acid or hippuric acid. In an acidic environment, methenamine is converted to formaldehyde, which is a nonspecific antimicrobial agent with bacteriocidal effects. It has activity against a variety of organisms, but is not effective against urease-producing microbes (e.g., *Staphylococcus, Proteus*, and *Ureaplasma*) that induce alkaluria. Mandelic and hippuric acid are used to acidify the urine. Methenamine is a safe drug but may cause gastrointestinal upset. It should not used in patients with diseases associated with metabolic acidosis (i.e., renal failure) because the drug is acidifying. For methenamine to be active, urine pH must be less than 6.0. This may require administering a urine-acidifying agent, such as vitamin C or d,l-methionine. The dosage for methenamine hippurate in dogs is 500 mg PO every 12 hours and for cats is 250 mg PO every 12 hours; dosage for methenamine mandelate is dogs is 10 to 20 mg/kg PO every 8 to 12 hours. It is not administered to cats because it causes side effects.

### Ancillary Therapy

Many forms of ancillary therapy have been recommended to aid in

treatment of UTI. Ancillary therapies include urinary acidifiers, urinary antiseptics, local instillation of antimicrobial agents into the urinary bladder, alteration of urine volume, and use of pharmacologic agents to affect the storage and voiding phases of micturition. Although the activity of antimicrobial agents is affected by urine pH, altering urine pH in an effort to increase activity is rarely done. An exception is inducing aciduria when the urinary antiseptic methenamine is used.

Instillation of antimicrobial agents into the urinary bladder is ineffective and may be associated with complications. For example, instillation of gentamicin into a compromised urinary bladder may result in absorption and achievement of toxic serum levels. If antimicrobial therapy is required, antimicrobials should be administered orally or parenterally. One example in which instillation of a pharmacologic agent into the urinary bladder may be beneficial is when a cystostomy catheter is used. The catheter is inserted directly into the urinary bladder and exits the ventral abdominal wall. Instillation of Tris-EDTA through the cystostomy catheter into the urinary bladder after the bladder has been emptied of urine may decrease the incidence of bacterial UTI (Bartges JW, Unpublished observation. 2003).

Cranberry juice or extract has been shown to exert bacteriostatic properties in humans; however, there are no data that document such benefits in dogs or cats. D-mannose has been recommended for *E. coli* infections on the basis that uropathogenic *E. coli* possess adhesion fimbriae that non-uropathogenic *E. coli* do not possess, and that D-mannose in a test tube blocks adhesion. However, this effect does not seem to occur in patients. Urinary acidifiers have been recommended to decrease recurrence of bacterial UTI; however, this is not effective in dogs and cats. Most bacteria can survive when the pH is between 5 and 9, and because dogs and cats cannot acidify their urine to less than 5.5, the level needed to prevent bacterial UTI cannot be achieved. None of these treatments is recommended.

### 7. Fix the Failure

Occasionally, antimicrobial therapy fails to eliminate a bacterial UTI. If treatment was based on urine culture, collected by appropriate methods and processed appropriately, then the first step is to ensure that the client and patient have been compliant. Noncompliance usually occurs due to communication errors. For example, the directions may read "give 1 tablet twice a day," resulting in the client giving the medication at 8 AM and at 2 PM rather than every 12 hours. Administration of the medication with or without food can also affect absorption. Some owners prematurely discontinue medication, resulting in a lack of clearance of the infection. In addition, the dog or cat may be noncompliant by not swallowing the pill or solution, resulting in subtherapeutic concentrations of the agent. Coexisting gastrointestinal disease (e.g., vomiting, diarrhea, or maldigestion/malabsorption) may interfere with drug absorption and cause treatment failure.

If the correct antimicrobial agent is administered at the appropriate dosage, then clinical signs should resolve within 2 to 3 days of beginning therapy. Failure of signs to resolve may be due to problems encountered with administration of the antimicrobial but may also occur if a mixed population of bacteria is present, if a super infection develops (a bacterial infection that develops while the patient is receiving an antimicrobial

agent), or if the existing bacteria develop antimicrobial resistance. Although most antimicrobial agents kill bacteria, some antimicrobials (e.g., chloramphenicol) are bacteriostatic. In animals with a compromised immune system, bacteriostatic antimicrobials may not be effective. Failure to clear a UTI may also occur in patients with predisposing factors that are not or cannot be corrected. For example, uroliths may harbor bacteria, resulting in treatment failure or relapsing infections. A search for predisposing causes should be made, and if identified, corrected if possible.

### Conclusion

Bacterial UTI is common in veterinary medicine. Appropriate treatment relies on a correct diagnosis and administration of an appropriate antimicrobial agent at the proper dosage and interval for the appropriate duration. Urine culture is the "gold standard" for diagnosis of a UTI; it provides speciation of the microorganism as well as antimicrobial sensitivity. In patients with recurrent UTI, further diagnostic testing is indicated. If a predisposing risk factor can be isolated, then it should be corrected, if possible. Lastly, prophylactic antimicrobial therapy may be required in some patients.

### References


1. Ling GV. Therapeutic strategies involving antimicrobial treatment of the canine urinary tract. J *Am Vet Med Assoc*. 1984;185:1162-1164.
2. Bartges JW. Bacterial urinary tract infections. In: Ettinger SJ, Feldman EC, eds. Textbook of Veterinary Internal Medicine. 6th edition. Philadelphia, Pa: W.B. Saunders Company; 2005:1800-1808.
3. Lulich JP, Osborne CA, Bartges JW, et al. Canine lower urinary tract disorders In: Ettinger SJ, Feldman EC, eds. Textbook of Veterinary Internal Medicine, 5th edition. Philadelphia, Pa: W.B. Saunders Company; 1999:1747-1783.
4. Lees GE. Bacterial urinary tract infections. Vet Clin North *Am Small Anim Pract*. 1996;26:297-304.
5. Thomsen MK, Svane LC, Poulsen PH. Canine uri-nary tract infection. Detection, prevalence and therapeutic consequences of bacteriuria. *Nord Vet Med*. 1986;38:394-402.
6. Lees GE. Epidemiology of naturally occurring feline bacterial urinary tract infections. *Vet Clin North Am Small Anim Pract*. 1984;14:471-479.
7. Bartges JW, Blanco L. Bacterial urinary tract infection in cats. *Compen Standard of Care*. 2001;3:1-5, 9.
8. Lekcharoensuk C, Osborne CA, Lulich JP. Epidemiologic study of risk factors for lower urinary tract diseases in cats. *J Am Vet Med Assoc.* 2001;218:1429-1435.
9. Vail DM, Allen TA, Weiser G. Applicability of leuko-cyte esterase test strip in detection of canine pyuria. *J Am Vet Med Assoc*. 1986;189:1451-1453.
10. Gerding PA, Jr., Morton LD, Dye JA. Ocular and dis-seminated candidiasis in an immunosuppressed cat. *J Am Vet Med Assoc*. 1994;204:1635-1638.
11. Forrester SD, Troy GC, Dalton MN, et al. Retrospective evaluation of urinary tract infection in 42 dogs with hyperadrenocorticism or diabetes mel-litus or both. *J Vet Intern Med*. 1999;13:557-560.
12. Pressler BM, Vaden SL, Lane IF, et al. Candida species urinary tract infections in 13 dogs and seven cats: predisposing factors, treatment, and outcome. *J Am Anim Hosp Assoc*. 2003;39:263-270.
13. Barsanti JA, Brown J, Marks A, et al. Relationship of lower urinary tract signs to seropositivity for feline immunodeficiency virus in cats. *J Vet Intern Med*. 1996;10:34-38.
14. Kruger JM, Osborne CA, Goyal SM, et al. Clinical evaluation of cats with lower urinary tract disease. *J Am Vet Med Assoc.* 1991;199:211-216.
15. Buffington CA, Chew DJ, Kendall MS, et al. Clinical evaluation of cats with nonobstructive urinary tract diseases. *J Am Vet Med Assoc*. 1997;210:46-50.
16. Lulich JP, Osborne CA. Bacterial urinary tract infections In: Ettinger SJ, Feldman

EC, eds. Textbook of Veterinary Internal Medicine, 4th edition. Philadelphia, Pa: W.B. Saunders Company; 1999;1775-1788.

17. Padilla J, Osborne CA, Ward GE. Effects of storage time and temperature on quantitative culture of canine urine. *J Am Vet Med Assoc*. 1981;178:1077-1081.
18. Carter JM, Klausner JS, Osborne CA, et al. Comparison of collection techniques for quantitative urine culture in dogs. *J Am Vet Med Assoc*. 1978;173:296-298.
19. Saunders A, Bartges JW, Bemis DA, et al. Evaluation of blood agar plates and incandescent lighting for aerobic bacterial urine cultures*. J Vet Intern Med*. 2002;16:379 (abstract).
20. Blanco LJ, Bartges JW, New J, et al. Evaluation of blood agar plates as a transport medium for aerobic bacterial urine cultures. *J Vet Intern Med*. 2001;15:303 (abstract).
21. Allen TA, Jones RL, Purvance J. Microbiologic evaluation of canine urine: direct microscopic examina-tion and preservation of specimen quality for culture. *J Am Vet Med Assoc*. 1987;190:1289-1291.
22. Barsanti JA, Johnson CA. Genitourinary infections In: Greene CE, ed. Infectious Diseases of the Dog and Cat. 2nd edition. Philadelphia, Pa: W.B. Saunders Company; 1990;157-183.
23. Osborne CA, Lees GE. Bacterial infections of the canine and feline urinary tract In: Osborne CA, Finco DR, eds. Canine and Feline Nephrology and Urology. Baltimore, Md: Williams & Wilkins; 1995:759-797.
24. Lees GE, Osborne CA, Stevens JB. Antibacterial properties of urine: Studies of feline urine specific gravity, osmolality, and pH. *J Am Anim Hosp Assoc*. 1979;15:135-141.
25. Freedman LR. Experimental pyelonephritis. 13. On the ability of water diuresis to induce susceptibility to E. coli bacteriuria in the normal rat. Yale *J Biol Med*. 1967;39:255-266.
26. Sofer S, Danon A, Gorodischer R. Effect of urine osmolality on the antibacterial activity of gentamicin. *Res Commun Chem Pathol Pharmacol*. 1983;41:323-332.
27. Oluoch AO, Kim CH, Weisiger RM, et al. Nonenteric Escherichia coli isolates from dogs: 674 cases (1990-1998). *J Am Vet Med Assoc*. 2001;218:381-384.
28. Adams WM, DiBartola SP. Radiographic and clinical features of pelvic bladder in the dog. *J Am Vet Med Assoc.* 1983;182:1212-1217.
29. Lavocat MP, Granjon D, Allard D, et al. Imaging of pyelonephritis. *Pediatr Radiol*. 1997;27:159-165.
30. Rushton HG, Majd M. Dimercaptosuccinic acid renal scintigraphy for the evaluation of pyelonephritis and scarring: a review of experi-mental and clinical studies. *J Urol*. 1992;148:1726-1732.
31. Buffington CA, Chew DJ, Kendall MS, et al. Clinical evaluation of cats with nonobstructive uri-nary tract disease. *J Am Vet Med Assoc*. 1997;210:46-50.
32. Wooley RE, Blue JL. Quantitative and bacteriologi-cal studies of urine specimens from canine and feline urinary tract infections. *J Clin Microbiol*. 1976;4:326-329.
33. Cohn LA, Gary AT, Fales WH, et al. Trends in flu-oroquinolone resistance of bacteria isolated from canine urinary tracts. *J Vet Diagn Invest*. 2003;15:338-343.
34. Ling GV, Norris CR, Franti CE, et al. Interrelations of organism prevalence, specimen collection method, and host age, sex, and breed among 8,354 canine urinary tract infections (1969-1995). *J Vet Intern Med*. 2001;15:341-347.
35. Davidson AP, Ling GV, Stevens E, et al. Urinary tract infection in cats: A retrospective study (1977-1989). California Vet. 1992;46:32.
36. Pellegrino R, Galvalisi U, Scavone P, et al. Evaluation of Proteus mirabilis structural fimbrial proteins as antigens against urinary tract infections. FEMS *Immunol Med Microbiol*. 2003; 36:103-110.
37. Cooke CL, Singer RS, Jang SS, et al. Enrofloxacin resistance in Escherichia coli isolated from dogs with urinary tract infections. J Am Vet Med Assoc. 2002;220:190-192.
38. Prescott JF, Hanna WJ, Reid-Smith R, et al. Antimicrobial drug use and resistance in dogs. *Can Vet J*. 2002;43:107-116.
39. Barsanti JA, Blue J, Edmunds J. Urinary tract infec-tion due to indwelling bladder catheters in dogs and cats. *J Am Vet Med Assoc.* 1985;187:384-388.
40. Osborne CA, Stevens JB. Urinalysis: A Clinical Guide to Compassionate Patient Care. Shawnee Mission, Ks: Bayer Corporation, 1999.

41. Seguin MA, Vaden SL, Altier C, et al. Persistent uri-nary tract infections and reinfections in 100 dogs (1989-1999). *J Vet Intern Med*. 2003;17:622-631.

*Date Published: January 10, 2008*







**800.700.4636 | VINGRAM@vin.com | 530.756.4881 | Fax: 530.756.6035**
**777 W. Covell Blvd, Davis, CA 95616**