Diagnosis and management of bacterial urinary tract infections in dogs and cats

Introduction

Clinical signs associated with lower urinary tract inflammation (inappropriate urination, dysuria, increased frequency) are common presenting complaints in small animal practice. These signs are most likely attributed to bacterial urinary tract infections in dogs and to sterile inflammatory conditions (e.g., feline idiopathic cystitis [FIC], urolithiasis) or behavioral disorders in cats. Bacterial urinary tract infections (UTIs) occur in approximately 14% of dogs in their lifetime,[1] with increased prevalence noted in older dogs.[2] In cats less than 10 years of age, bacterial UTI is uncommon, affecting only 1%–8% of this population.[3–5] UTI is seen more often in older cats and in cats with chronic kidney disease (CKD) or a history of urinary tract procedures.[6–9] Upper urinary tract infection, or pyelonephritis, is less prevalent in companion animals, but it is clinically important because of the potential sequelae for significant kidney damage and both acute kidney injury and chronic kidney disease.

Successful treatment of UTI begins with an accurate diagnosis of infection. An antibiotic regimen should be chosen that is appropriate to treat both the bacteria identified and the patient that has been clinically assessed for preexisting complicating factors or conditions. Patients with signs of lower urinary tract disease or otherwise suspected of UTI should have a complete urinalysis (UA) performed on a fresh urine specimen, with emphasis on a detailed microscopic urine sediment examination. The urine specimen should be collected aseptically by cystocentesis. A quantitative urine culture with minimum inhibitory concentration (MIC) antibiotic susceptibility testing is recommended to confirm bacteriuria identified on UA and to guide antibiotic selection. This is especially important for patients with complicated UTIs.

Most UTIs are the result of ascending bacteria from rectal or fecal contamination or from the distal urogenital tract. A single species of Gram-negative bacteria is cultured from most UTIs, typically *E. coli*, with Gram-positive *Staphylococcus*, *Streptococcus*, and *Enterococcus* infections and mixed-bacterial infections reported less frequently.[10,11] Familiarity with the most common urinary pathogens, along with bacterial morphology identified by urine sediment examination may help to guide initial treatment while culture results are pending. **Effective April 2017, in addition to reporting presence of rare, moderate or marked bacteria, IDEXX Reference Laboratories will report the morphology (rods, cocci) of any bacteria present on your urinalysis results.**

Predisposing factors for bacterial UTI

In dogs, predisposing factors for bacterial UTI include, but are not limited to, gender (being a spayed female); anatomic or functional changes that influence continence or complete emptying of the bladder, such as ectopic ureters[12] and posterior paresis[13]; systemic diseases, such as diabetes mellitus, hyperadrenocorticism,[14] and hyperparathyroidism[15]; or the use of medications such as glucocorticoids.[16] UTIs are common in cats with concurrent chronic kidney disease, diabetes mellitus, and hyperthyroidism.[17,18]

Clinical signs

The clinical signs seen with UTI vary depending on the part of the urinary tract affected. Infections of the upper urinary tract (pyelonephritis) that involve the kidney and adjacent ureters may result in systemic signs of illness, including fever, depression, anorexia and vomiting, and flank or renal pain. Localized infections of the lower urinary tract are recognized more commonly with bladder infection causing cystitis, which is often combined with urethral infection, or urethrocystitis.

Common signs of lower urinary tract infection include frequent voiding of urine (pollakiuria) with dysuria, marked by urgency and straining (stranguria), as well as urinary accidents or urinating in inappropriate places (periuria; e.g., outside the litter box). Affected animals may urinate cloudy or grossly bloody urine (hematuria) that is sometimes malodorous. They may lick at the urogenital area, cry or vocalize, or develop urinary incontinence. In contrast to upper urinary tract infection, systemic signs of illness are not expected with lower urinary tract infections.[19] Clinical signs of UTI may be subtle or are unrecognizable in some patients that have an infection confirmed by urine culture.[20]

Asymptomatic, simple, and complicated urinary tract infections

Determining the clinical significance of confirmed bacteriuria in a patient without clinical signs of UTI, e.g., with asymptomatic bacteriuria[19] or subclinical bacteriuria, should include a thorough consideration of all patient factors and information about the potential for pathogenicity of the bacteria cultured.[21,22] Veterinarians may tend toward overdiagnosis to avoid missing UTI with subtle clinical signs, but treatment may not always be indicated for subclinical bacteriuria.[22] Consultation with a veterinary internist or microbiologist may be helpful in determining whether treatment could be warranted in a patient not exhibiting clinical signs of a UTI.

For patients with clinical signs, UTI management may differ depending on whether the infection is a simple, uncomplicated UTI or a complicated UTI. Simple UTIs are sporadic or infrequent bladder infections (typically no more often than two to three times a year) diagnosed in a female or neutered male dog that is otherwise healthy and has normal urinary anatomy and function.[21,23] This patient group is often successfully treated with first-line antibiotics without guidance from a urine culture.

Complicated UTIs include infections in patients with concurrent predisposing condition(s), as well as infections in cats and intact male dogs.[23] Diagnosis and effective management of complicated UTI generally requires both a complete urinalysis and quantitative culture and susceptibility testing. When possible, predisposing cause(s) should be determined concurrently with a comprehensive workup that includes a complete CBC and biochemistry with electrolytes and the IDEXX SDMA® Test, and may also include advanced imaging of the urinary tract. Endocrine function testing

or other diagnostics may be necessary. Treating or correcting the underlying cause(s) where possible is also needed to increase the chances of microbial cure. Monitoring the success of treatment of complicated UTIs is another routine indication for urine culture.

Recurrent infections are complicated UTIs. Urine culture results are needed to differentiate between persistent or relapsing infections with the same organism and reinfections that are associated with a different microorganism than was previously isolated.[21] Diagnostic workup for patients with recurrent UTIs may be similar, but management is typically quite different for patients with persistent infections versus new infections. Patient advocacy and responsible stewardship of antibiotic use should motivate veterinary professionals to understand the success of antimicrobial treatment and to investigate the reasons for any apparent failure of treatment. The use of culture and sensitivity testing results to carefully guide antibiotic usage is one strategy to limit the antimicrobial resistance problem that exists today.[24]

Diagnosis of urinary tract infections

A complete urinalysis, consisting of physical and chemical evaluations, and microscopic examination of an unstained, wet urine preparation may suggest a probable diagnosis of UTI, facilitating timely treatment of a painful and possibly life-threatening condition. Microscopic identification of bacteria on UA is not in itself diagnostic for UTI. Consistent clinical signs and history or other supportive evidence of infection, such as pyuria or hematuria on microscopic examination, are needed for a diagnosis of UTI. Inflammation can occur for reasons other than bacterial infection, for example, patients with FIC, urolithiasis, or tumors may have inflammatory cells present in their urine, but they may not have concurrent bacterial infections. Chemical findings (e.g., blood or protein on dipstick) suggestive of inflammation should always be confirmed with a microscopic urine sediment examination (see figure 1). Chemical estimations of leukocytes are invalid in cats and only occasionally valid in dogs on urine dipsticks, so they must always be confirmed cytologically.
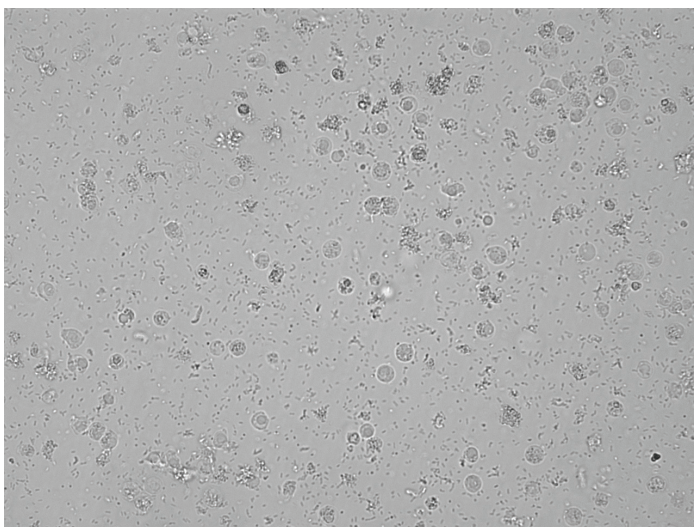

Figure 1. Active urinary sediment demonstrating bacteriuria and increased white blood cells. Image is provided by IDEXX SediVue Dx® Urine Sediment Analyzer.

Quantitative urine culture is recommended to identify and quantify bacteria, allowing assessment of clinical significance relative to collection method and facilitating differentiation between contamination and UTI. The minimum inhibitory concentration (MIC) susceptibility results are used to guide effective therapy by selection of an appropriate antibiotic and dosing range. Presumptive antibiotic treatment can be started while the results of a quantitative urine culture with MIC susceptibility testing are pending.

Using bacterial morphology to guide initial therapy

Microscopic assessment of bacterial morphology as rods or cocci as well as semiquantitative bacterial counts may be useful to guide initial antibiotic use or empiric treatment. The aerobic rod-shaped bacteria frequently recovered from urine, such as *E. coli*, *Proteus, Klebsiella*, and *Enterobacter*,[19] are often successfully treated with bactericidal beta-lactam antibiotics (aminopenicillins, cephalosporins, carbapenems), trimethoprim/sulfas or fluoroquinolones. Anaerobic, rod-shaped bacilli, such as *Clostridium*, are rarely causative agents of UTIs.[19] *Staphylococcus* are aerobic cocci that typically respond to treatment with most beta-lactams unless they are drug-resistant strains. *Enterococcus* is a facultative anaerobic diplococcus, which may be confused with *Streptococcus* and is often difficult to treat because clinically effective antibiotic choices are limited. Aminopenicillins, such as amoxicillin, amoxicillin/clavulanic acid, and ampicillin, are considered the drugs of choice for treating *Enterococcus* unless it is identified as a multiple-drug-resistant infection based on culture and susceptibility testing.

Use of Wright's stain to improve accuracy

Rods and/or cocci in chains (see figure 2) can be confidently identified by trained technicians, however specimens with ambiguous bacterial morphology, with low bacterial numbers or with low specific gravity[25] may confound accurate reporting. Rods are readily detected with quantitative bacterial counts >10,000 colony-forming units (cfu)/mL, while the smaller cocci require counts ≥100,000 cfu/mL for consistent detection.[26] False-positive reports of bacteria are considered common with unstained specimens, resulting in discordant results between culture and urine sediment examinations performed by trained observers.[27–29] Lipid droplets, amorphous crystals, debris, or cytoplasmic organelles may present as pseudobacteria that are incorrectly identified as bacteria in an unstained specimen (see figure 3).[29]
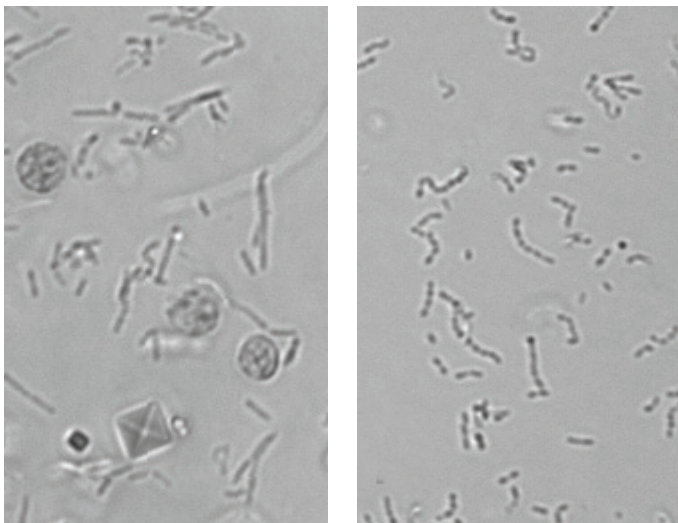
Figure 2. Identification of bacteria on urine sediment, from left to right, rods, cocci in chains. Images are provided by IDEXX SediVue Dx® Urine Sediment Analyzer.
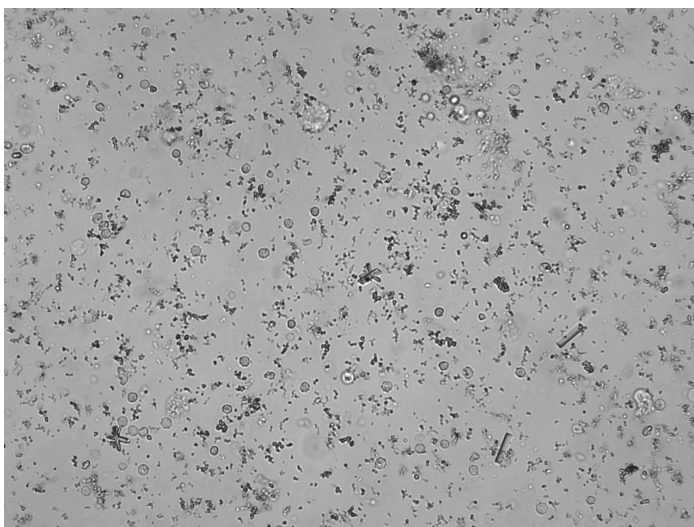

Figure 3. Amorphous debris masquerading as bacteria. Image is provided by IDEXX SediVue Dx Urine Sediment Analyzer.

Modified Wright's-stained preparations of air-dried urine sediment improves accuracy of bacterial reporting over routine unstained methods, when they are compared to the gold standard method of quantitative bacterial culture.[27,29] Interpretation of Wright's-stained canine specimens yielded excellent sensitivity (93.2%), specificity (99.0%), and positive (94.5%) and negative (98.7%), predictive values.[27]

A similar study in cats determined that air-dried stained urine specimens were more accurate than wet-unstained preparations, with an improved sensitivity, specificity, and classification of bacteriuria.[29] The authors concluded that the modified Wright's-stained preparation was a rapid, easy, and cost-effective way to enhance recognition of bacteriuria in cats or dogs[27,29] and was a superior methodology to traditional Gram-staining in dogs.[27]

To minimize the risk of false-positive bacteria reporting and to aid in accurate morphological identification, IDEXX Reference Laboratories utilizes Wright's stain to confirm suspect or ambiguous bacteria present in urinalyses.

Understanding discordancies between urinalysis and culture

Even when best practices are followed, discordance between a urine sediment examination and culture results may occur. The most likely explanations for a discrepancy in microscopic examination and reporting of a positive identification of bacteria on UA and a negative urine culture result on the same specimen include the following:

• Bacteria may have been visualized microscopically but may be dead (nonviable), especially if the animal is currently on antibiotics or had previously or recently been treated with antibiotics at the time of specimen collection. Other factors that may inhibit or prevent bacteria growth in culture include exposure of the specimen to temperature extremes, extremes of urine pH (≤4 or ≥9),[30] or inhibition by white blood cells (in urine with "too numerous to count" white blood cells).

• The "organisms" identified with microscopy could have been cellular debris in the urine that was misidentified as bacteria, called pseudobacteria (particularly with unstained urine sediment examination).

• Random motion of small colloidal particles, known as Brownian motion, can falsely appear to be cocci bacteria (particularly with unstained urine sediment examination).

• Rarely, anaerobic bacteria may be visualized on UA but not grown in aerobic cultures.

• If the urine specimen was stained in-clinic prior to microscopic examination, the stain may have been contaminated with bacteria. Stains should be changed regularly.

It is possible to have a positive urine culture without identifying bacteria on the urinalysis. A negative bacteria result on UA in combination with positive urine culture can be seen when bacterial numbers are too low to be consistently visualized on UA, for example in very dilute urine, following incompletely successful antibiotic therapy or in the case of localized pyelonephritis. In situations where the clinical history is suggestive of urinary tract infection or an active urine sediment is present, urine culture should be considered even in the absence of bacteriuria on urinalysis.

Using urine cultures to maximize therapeutic success

Quantitative aerobic urine culture remains the gold standard for the diagnosis of UTI. Bacteria identified in the urine may represent contamination from the distal urogenital tract, the gastrointestinal tract, or the skin surface, rather than UTI. After confirming probable bacteriuria with a Wright's stain, a quantitative urine culture on a pretreatment specimen collected aseptically by cystocentesis is the best way to confirm significant bacteriuria. The identity and level of bacterial growth helps to establish clinical relevance. Quantitative criteria for determining infection in urine specimens based on their source are commonly referenced but must be interpreted in light of other clinical findings, such as clinical signs of UTI, urinalysis findings, patient history, and possible problems with the procedure or specimen handling:[19]

Source	Contamination (bacteria/mL)	Infection
Midstream voided	$<10^5$	Not discriminatory in dogs; $>10^5$ in cats
Catheterization	$<10^3$ in male dogs and cats, any number in female dogs	$>10^4$ in male dogs $>10^3$ in cats, any number in cats with indwelling catheters
Cystocentesis	$<10^3$	$>10^3$

This data highlights the importance of proper urine specimen collection. Cultures of specimens collected by voiding are difficult to interpret since they have the potential for high-level contamination, thus cystocentesis specimens are best practice. Specimens collected by sterile catheters are acceptable for use in all but female dogs. Positive culture results from voided specimens should be confirmed on a cystocentesis specimen unless medically contraindicated.[21] Specific contraindications to cystocentesis include bleeding disorders, coagulopathies, and the presence of bladder cancer, such as transitional cell carcinoma, which may be transplanted by needle puncture. Urinary obstruction may be considered a relative contraindication, since therapeutic bladder decompression by cystocentesis has been described.[31]

Fresh urine specimens should be submitted to the reference laboratory for aerobic culture in a sterile container, such as a plain plastic tube (WTT) or other non-additive sterile tube, within 24–36 hours of collection. Specimens should be refrigerated until submission. Yellow-top urine culture tubes that contain boric acid should only be used when a significant delay in submission is expected. These tubes must be properly filled to prevent suppression of culture growth and maintained at room temperature until the time of submission. Recent antibiotic therapy, within the previous 2 weeks, may result in lower yield or negative urine cultures. Withdrawal from antibiotics for a minimum of 72 hours, ideally 7–10 days, is recommended when culturing a patient following antibiotic administration.

Complete urine culture with susceptibility results are typically available within 48 hours, depending on organism growth. If empiric antibiotic therapy was initiated while awaiting results, it is usually best to continue treatment with the initial antibiotic if the patient is showing clinical improvement and susceptibility results support the continued use of that antibiotic. If the animal is not receiving antibiotics, or if the organism grown is only partially susceptible or is resistant to the antibiotic selected, the choice of antibiotics and length of therapy should be based on an evaluation of the antibiotic susceptibility results in combination with other patient factors, including site of infection (cystitis versus pyelonephritis), presence of predisposing factors, assessment of simple versus complicated infection, and prior antibiotic use. To learn more about using the minimum inhibitory concentration (MIC) on your susceptibility results to guide your antibiotic choice, visit **idexx.com/MIC**.

Ordering information

Test code	Test name and contents

910
9101 **Urinalysis**
Add-on

Physical, chemical, and microscopic analyses

4035 **Urine Culture and MIC Susceptibility**

Organism ID and susceptibility

1394 **Urinalysis, Urine Culture and MIC Susceptibility**

Urinalysis: physical, chemical, and microscopic analyses

Urine culture: Organism ID and susceptibility

Note: Urine culture is performed regardless of findings of urinalysis.

3901 **Urinalysis with Urine Culture and MIC Susceptibility (if Indicated)**

Urinalysis with reflex urine culture if indicated. If the urinalysis has a low specific gravity (≤1.015), has white blood cells (>5/hpf), and/or bacteria are seen, a urine culture will be automatically run at no additional charge.

Note: The test price is the same whether a urine culture is performed or not.

9430 **Urine Culture and MIC Susceptibility (if Indicated) Add-on**

Add-on to a urinalysis or a profile containing a urinalysis.

If the urinalysis has a low specific gravity (≤1.015), has white blood cells (>5/hpf), and/or bacteria are seen, a urine culture will be automatically run at no additional charge.

Note: The test price is the same whether a urine culture is performed or not. Must be ordered concurrent with a urinalysis.

Specimen requirements: 5 mL urine in a sterile container (for culture collection by cystocentesis and submission in a WTT preferred)

Turnaround time: 8:00 a.m. for urinalysis; preliminary culture results in 1–2 working days

Contacting IDEXX

1-888-433-9987
For questions regarding sample submission or test results, please contact our Laboratory Customer Support Team. For questions regarding individual patient management, please contact our Medical Specialty Consulting Services Team.

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