SA316

URINE HEAVEN: OF BUGS & DRUGS – URINARY TRACT INFECTIONS

Joe Bartges, DVM, PhD, DACVIM, DACVN
The University of Tennessee
Knoxville, Tennessee, USA

A bacterial urinary tract infection (UTI) exists when bacteria adhere, multiply, and persist in a portion of the urinary tract. The infection may or may not produce clinical signs. Bacterial urinary tract infections are reported to occur in 2-3% of dogs and in less than 1% of cats. Cats appear to be more innately resistant to bacterial UTI than dogs. The urinary tract is in contact with the external environment and has many defense mechanisms to prevent bacterial UTI.

Physical examination findings and clinical signs

Clinically, bacterial urinary tract infections may be symptomatic or asymptomatic. Bacterial infection of the lower urinary tract is usually associated with clinical signs that are similar to other diseases of the lower urinary tract. These signs include, but are not limited to, pollakiuria, dysuria, stranguria, hematuria, and inappropriate urination. Bacterial urinary tract infection of the kidneys may be associated with hematuria, or if septicemia develops, the animal may be systemically ill. In addition, upper urinary tract infections may cause recurrent lower urinary tract infections.

Diagnosis

Urinalysis and Urine Culture

Evaluating results of a complete urinalysis of a sample collected by cystocentesis is the best way to screen for bacterial UTI. Some dipsticks contain reagent pads for nitrate or leukocyte esterase activity; however, these pads are not reliable for ruling-in or ruling-out bacterial UTI in dogs and cats. A urine sediment examination should always be performed as part of a complete urinalysis. Presence of pyuria (> 5 white blood cells / high-powered field) is important because other causes of lower urinary tract disease are associated with hematuria and proteinuria but minimal pyuria. Identification of bacteria on urine sediment examination is helpful; however, it should not be relied upon to rule-in or rule-out bacterial UTI. Evaluating a modified Wright's stain urine sediment preparation is a cost-effective and easy method that provides more reproducible and accurate results than evaluating an unstained urine sediment preparation. A urine culture is the most definitive means of diagnosing bacterial UTI. Care must be taken to collect, preserve, and transport the urine sample to avoid contamination, or proliferation or death of bacteria. Urine specimens for aerobic bacterial culture should be transported and stored in sealed, sterilized containers, and processing should begin as soon as possible. If laboratory processing is delayed by more than 30 minutes, the specimen should be refrigerated (4 C). Blood agar plates may be inoculated and incubated for 24 hours. If bacteria are present on the plate after 24 hours, the plate may be submitted for identification and determination of antibiotic sensitivities. The most common technique used for determining antimicrobial susceptibility is the Kirby-Bauer agar diffusion test. After an organism is isolated, it is streaked on an agar plate and antimicrobial discs are placed on the plate.

Bacteria that commonly cause UTI are the same in dogs and cats. Infections caused by Escherichia coli are the most common, accounting for one-third to one-half of all organisms isolated from the urine of infected animals. Gram-positive cocci are the second major group of organisms. Staphylococci and streptococci account for one-fourth to one-third of the isolates recovered. Bacteria that cause the remaining one-fourth to one-third of urinary tract infections include Proteus spp., Klebsiella spp., Pasteurella spp., Enterobacter spp., Pseudomonas spp., Corynebacterium spp., and Mycoplasma spp.; however, these are uncommon.

Treatment

Treatment of bacterial UTI is dependent upon whether the infection occurs due to a temporary breech in the body's defense mechanisms (uncomplicated) or whether there is an irreversible breech in the defense mechanisms (complicated). Eradication of bacterial urinary tract infection is dependent on selection of the appropriate antibiotic, administering it at the proper dosage and duration, and appropriate follow-up.

Uncomplicated bacterial UTI

Uncomplicated bacterial UTI are those where no underlying structural, neurologic, or functional abnormality is identified. Uncomplicated bacterial UTI are usually successfully treated with a 10-14 day course of an appropriate antimicrobial agent. If the proper antibiotic is chosen and administered at the appropriate dosage and frequency, clinical signs should resolve within 48 hours. Additionally, results of a complete urinalysis should improve within this same time frame. If possible, a urine culture should be performed 5-7 days after cessation of antimicrobial therapy in order to ensure eradication of the UTI.

Complicated bacterial UTI

A complicated UTI occurs when the break in host defenses whether local or systemic is permanent or cannot be corrected or controlled and/or when a bacterial organism persists or is highly resistant to antimicrobial agents or a combination of the two. Reproductively intact dogs, all cats, and animals with identifiable predisposing causes for bacterial UTI (e.g. renal failure, hyperadrenocorticism, diabetes mellitus, etc) should be considered to have a complicated bacterial UTI. Pyelonephritis and prostatitis are examples of complicated bacterial UTI. When a cat is confirmed with a bacterial UTI, they should be treated as a complicated UTI because cats are inherently resistant to development of an infection. Treatment with antibiotics for longer than the routine 10 to 14 days may be indicated, and are usually administered for 4-6 weeks. Urine should be evaluated in the first week of treatment for response to therapy and prior to discontinuing therapy. After antimicrobial therapy is discontinued, urine should be cultured 5-7 days later. Use of once a day antibiotic treatment may be necessary in order to control bacterial urinary tract infections that are difficult to eradicate.

Management of recurrent complicated bacterial UTI – Recurrent UTI's may occur with noncompliance by the owners or dog/cat. In patients with recurrent UTI, a urine culture should always be performed in order to identify whether a UTI is present and to determine what anti-microbial agents may be used. If predisposing breaks in host defenses are identified, correction or control of them may aid in treatment and prevention.

Resistant E coli UTI – Several options may exist depending on results of culture and sensitivity:

- Fluoroquinolones: May be effective when used at high dosage (e.g. enrofloxacin: 5-20 mg/kg PO q24h)
- Aminoglycosides: Are often an effective antimicrobial agent. Amikacin appears to be less associated with nephrotoxicity than gentamycin, but should not be given to animals with azotemia. It can be administered by owners at home (cats: 10-15 mg/kg IV, IM, SQ q24h; dogs: 15-30 mg/kg IV, IM, SQ q24h)
- Potentiated beta-lactams: may be tried if intermediate susceptibility is present. I usually use amoxicillin-clavulanic acid at a higher dosage (22 mg/kg PO q12h). Ampicillin-sulbactam may also be used (cats - 20-30 mg/kg PO q8-12h x 3-7 days; 5-11 mg/kg IM, SQ q8-12h; has been given 20-40 mg/kg IV q6-8h; dogs - 12.5 – 30 mg/kg PO q8-12h x 7 days; 6.6 -40 mg/kg IM, SQ q16-2h x 3-7 days; has been given 20-40 mg/kg IVq6-8h)
- Penems: Meropenem may be useful for highly resistant infections (8 mg/kg SQ q12h)
- 3rd generation cephalosporins: May be useful. Cefpodoxime (Simplicef) does not have as much activity as parenteral forms and may not be effective even with a favorable sensitivity pattern (5-10 mg/kg PO q24h).
- Cefovecin: A newer parternal long-acting cephalosporin has been shown to be effective against E coli in dogs and cats; however, effectiveness with resistant organisms is unknown (8 mg/kg SQ q14d)

Staphylococcus UTI (methicillin resistant) – These appear to be more difficult to treat. With resistance to methicillin, beta lactam antibiotics even potentiated ones will not be effective. Staphylococci are inherently resistant to fluoroquinolones (as are most Gram positive cocci) even with a favorable sensitivity pattern.

- Chloramphenicol: 50 mg/kg PO q8h; monitor liver enzymes as can be hepatotoxic, GI side effects occur commonly
- Linezolid: An oxazolidinone antibiotic with activity against Gram + organisms. It is often effective against methicillin-resistant Staphylococci, but is expensive (10 mg/kg PO q12h)
- Vancomycin: Standard for treating methicillin-resistant Staphylococci, it is discouraged from being use because of potential for inducing resistance that may spread to human medicine (15 mg/kg IV q8h).

Enterococcus UTI - Oftentimes Enterococcus UTI is not associated with clinical signs and there is suggestion that not treating may be better than treating. In some animals without clinical signs or urinalysis changes (pyuria, hematuria), no treatment with re-culture in 2 weeks may reveal eradication of the organism. Treatment should be considered for animals with active clinical infection or that are immunocompromised.

- Penicillins: may be sensitive to amoxicillin/ampicillin especially potentiated ones at higher dosages
- Inherently resistant to cephalosporins, fluoroquinolones, trimethoprim-sulfa, erythromycin even if favorable sensitivity results
- Can combine amikacin with a penicillin
- Penems may be effective for E faecalis, but not E faecium infections
- Linezolid and vancomyin may be effective

Prevention

Bacterial UTI can be prevented by minimizing bacterial contamination of the urinary tract and by avoiding or minimizing conditions that impair host defenses. Catheterization and endoscopy of the urinary tract always carry a risk of inducing an infection. The magnitude of the risk increases with the degree of pre-existing urinary tract abnormality, the amount of any additional injury caused by the procedure, and the duration of the procedure. These risks of infection can be minimized by being careful to perform invasive procedures only when necessary, by performing the procedure as atraumatically as possible, and by removing the catheter or endoscope as soon as possible. Cats with perineal urethrostomies are also at higher risk for developing bacterial urinary tract infections compared with cats without perineal urethrostomies; thus, other therapeutic interventions should be tried before resorting to this procedure.

Catheter-induced bacterial UTI present a common problem encountered by veterinarians. Bacteria may migrate along the outside of the catheter or through the lumen. Risk of bacterial UTI increases with pre-existing urinary tract disease or urothelial damage. The risk is greater in animals with indwelling urethral catheters when compared with animals that are intermittently catheterized.[11] Despite this lower risk, one study documented bacterial UTI in 7 of 35 dogs that were catheterized one time. Bacterial UTI occurs in >50% of animals after 4 days of an indwelling urethral catheter. Antibiotic therapy while an indwelling catheter is in place decreases the frequency of bacterial UTI; however, when bacterial UTI occur, the organisms exhibit a greater degree of antimicrobial resistance. Catheter-associated bacterial UTI may be minimized by using intermittent catheterization when possible, removing indwelling catheters as soon as possible, using a closed collection system, and avoiding administering antimicrobial agents while urethral catheters are inserted.

Prophylactic antimicrobial therapy may be indicated in animals with relapses or frequent reinfections. The antimicrobial agent should be selected based on urine bacterial culture and susceptibility testing. The agent is administered at ½ to $^1/_3$ of the daily therapeutic dose, and is usually administered once a day at night. For Gram + organisms, consider amoxicillin (22 mg/kg PO q24h). For Gram – organisms consider a first generation cephalosporin (22 mg/kg PO q24h) or nitrofurantoin (4 mg/kg PO q24h). Urine should be re-cultured every 4-6 weeks to insure control of the bacterial UTI. Experience has shown that if animal does not have a "break-through" infection during a 6-month period, then antimicrobial therapy may be successfully discontinued. Disadvantages of this approach include development of resistant bacteria and side effects of the antimicrobial agent. An alternative to prophylactic antimicrobial therapy in dogs is administration of methenamine. **Methenamine** (hippurate: cats – 250 mg PO q12h; dogs – 250-500 mg PO q12h) is a urinary tract antiseptic that is effective when the urine pH is less than 6.0. It is used for prophylaxis and requires a sterile urine culture prior to use. Because it requires an acidic urine pH, it is contraindicated in dogs with metabolic diseases associated with metabolic acidosis (e.g. chronic renal failure and diabetic ketoacidosis); cats do not tolerate methenamine as well as dogs. In addition, methenamine will not be effective with bacterial UTI that involve urease-producing microbes that are associated with alkaluria. It may be necessary to administer a urinary acidifier (e.g. vitamin C or d,l-methionine) to achieve a urine pH < 6.0. In female dogs with recurrent vaginocystitis, **estrogens** may be used with the idea that they promote turnover of vaginal epithelium and may decrease bacterial colonization of the vaginal cavity resulting in decreased cystitis.

Probiotics may alter GI flora and decrease numbers and types of bacteria in the urogenital

tract. Use a probiotic that contains multiple organisms at highest numbers. I typically use VSL#3 (www.vsl3.com) as it contains 450 billion organisms (8 different ones) per packet. The web site contains a dosing suggestion based on body weight (children) that is used to adjust dosage for animals (e.g. a cat often receives 1/10 of a packet per day = 45 billion live organisms). The veterinary probiotic Proviable (Nutramax Laboratories) is also a multi-organism product containing 5 billion organisms per capsule. Recently, a product containing **proanthocyanidins**, which are the active compound of cranberries that prevent adhesion of bacteria (particularly E coli) has become available (Crananidin, Nutramax Laboratories). Studies in humans show effectiveness in prevention of UTI; however, data are lacking in dogs.