BACTERIAL URINARY TRACT INFECTIONS

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INTRODUCTION AND INCIDENCE

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 to 3% of dogs and in less than 1% of cats.[1,2] 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.[3] Anatomically, the length of the urethra, presence of high pressure zones within the urethra, urethral and ureteral peristalsis, vesicoureteral flaps to prevent reflux of urine from the bladder into the ureters, and extensive renal blood supply and flow are protective. Mucosal defense barriers that prevent migration of bacteria and subsequent colonization include the presence of a glycosaminoglycan layer, antibodies, intrinsic mucosal antimicrobial properties, exfoliation of cells, and bacterial interference by commensal microbes of the distal urethra and distal genital tract. The composition of the urine also aids in prevention of development of bacterial urinary tract infection. Urine produced by cats is normally concentrated, oftentimes having a specific gravity >1.045 with an associated high osmolality.[4] Urine also contains substances that are inhibitory to bacterial colonization including high urea concentration, and presence of organic acids, low-molecular weight carbohydrates, and Tamm-Horsfall mucoprotein. Cell-mediated and humoral-mediated immunity present within the urine or urinary tract also impart protection. Frequent and complete voiding also helps to wash out bacteria that have migrated into the bladder, ureters, and kidneys.

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.[5] Urine specific gravity may be normal; however, dilute urine may be a risk factor for development of bacterial UTI or a consequence of an upper urinary tract infection.

A urine culture is the most definitive means of diagnosing bacterial UTI.[6] 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 (4ºC). 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.[7,8]

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. This test is based on attainable antimicrobial concentrations in human plasma and the assumption is that plasma concentrations are similar between species. However, many antibiotics attain higher concentrations in urine than in plasma; therefore, this technique may underestimate a microbe's susceptibility to antimicrobials. A more sensitive and specific technique is to determine the minimum inhibitory concentration (MIC). The MIC is the lowest concentration of antimicrobial required to inhibit bacterial growth. It is performed using a series of dilutions of each antibiotic in a multi-well plate to which a standard number of bacteria are added. Although this is a better test, it is more expensive and for most bacterial isolates, the Kirby-Bauer method is acceptable.

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.

Unless septicemia is present, results of a CBC should be normal. If septicemia is present, leukocytosis and a left shift may be present. Bacterial infection of the lower urinary tract does not cause changes in serum biochemical analysis. In animals with pyelonephritis, serum biochemical analysis may be normal if only one kidney is infected or if minimal damage has occurred, or it may reveal biochemical changes consistent with renal failure. Hyperthyroidism has also been associated with inducing a diuresis and bacterial urinary tract infections in cats. Additional laboratory evaluation of cats may include testing for Feline Leukemia Virus and Feline Immunodeficiency Virus, which may compromise the immune system.

Radiography, Ultrasonography, and Endoscopy

In many animals with bacterial urinary tract infections, radiography will be normal. However, survey radiography may reveal uroliths, renomegaly, or other defects that may predispose to development of bacterial urinary tract infection. If no abnormalities are found by survey abdominal radiography, ultrasonography or contrast radiography should be performed. The upper urinary tract may be evaluated by use of excretory urography;[9] whereas, the lower urinary tract may be evaluated by use of contrast cystography and urethrography, and double contrast cystography. A disadvantage of performing contrast radiography of the lower urinary tract is risk of inducing bacterial urinary tract infections during catheterization. Ultrasonography is a non-invasive technique and can evaluate the kidneys and bladder; however, its use is limited for evaluating the ureters and majority of the urethra.

Endoscopy of the lower urinary tract may be useful in identifying mucosal and intra-luminal lesions of the urinary tract, which may predispose to bacterial infection. In one study, a urolith not visible by survey radiography was visualized during cystoscopy.[10] Disadvantages of cystourethroscopy include requiring anesthesia to perform the procedure, invasion of the lower urinary tract which may compromise host defense mechanisms, and difficulty of performing the procedure in male cats without perineal urethrostomies.

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- to 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 to 7 days after cessation of antimicrobial therapy in order to ensure eradication of the UTI.

Complicated Bacterial UTI

Reproductively intact dogs, all cats, and animals with identifiable predisposing causes for bacterial UTI (eg, renal failure, hyperadrenocorticism, diabetes mellitus) 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 to 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 to 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.

Recurrence of Bacterial UTI

Relapse – A relapse is defined as recurrence of a bacterial UTI due to the same organism. Relapses usually occur within days to weeks of discontinuing 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 prior to re-instituting antimicrobial therapy. Additionally, further diagnostic evaluation may be warranted.

Reinfection – A reinfection is defined as an infection with a different organism than what was initially present. Reinfections usually occur weeks to years 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 bacterial UTI. However, if reinfections occur at a frequency of >3 per year, then animals should be treated as having a complicated bacterial UTI. Additionally, prophylactic antimicrobial therapy may be warranted.

Superinfections – A superinfection occurs when a second bacterial organism is isolated while an animal is receiving antimicrobial therapy. Oftentimes, this organism displays a high degree of antibiotic resistance. A bacterial UTI that occurs in animals receiving antimicrobial therapy that also have an indwelling urethral catheter is an example of a superinfection.[11]

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;[12,13] 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.[14] 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. Urine should be re-cultured every 4 to 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 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.

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