Difficult urinary tract infections

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The great majority of urinary tract infections (UTIs) are benign and readily respond to antimicrobial therapy. However, some patients fail to respond to antimicrobial therapy or develop recurrent UTIs following withdrawal of antimicrobial therapy. Recurrence of clinical and/or laboratory signs of UTI may occur as a consequence of relapse (persistent infection), reinfection, or superinfection. Classifying recurrent UTI in this fashion is clinically useful because it provides guidance as to the possible cause for recurrent UTI.

The type of recurrence can usually be established by comparing the results of follow-up urine cultures to results of the pre-treatment urine culture. Relapses (persistent infections) are defined as recurrences caused by the same species and serologic strain of microorganism(s) shortly after cessation of antimicrobial therapy (usually within several days to weeks). Urine cultures may or may not be sterile immediately following treatment. In contrast, reinfections are recurrent infections caused by a pathogen different from that causing the previous infection. Reinfections usually occur at a longer interval after cessation of antimicrobial therapy, and urine cultures are typically sterile immediately following initial treatment. Reinfections are the most common form of recurrent UTI. Superinfections, a relatively uncommon form of recurrent UTI, are new infections which develop during the course of antimicrobial therapy. Urine cultures will be positive during or immediately after terminating therapy.

Confirming the Diagnosis of Bacterial UTI: A presumptive diagnosis of UTI is often based on clinical and urinalysis findings. Detection of pyuria and bacteriuria by urine sediment evaluation is highly suggestive of bacterial UTI. However, bacteria are more difficult to detect in urine than are white blood cells; therefore, their absence does not exclude a diagnosis of bacterial UTI. The diagnosis of UTI should be confirmed by urine culture because diagnosis based solely on clinical signs and the presence of inflammatory changes on urinalysis (white and/or red blood cells and protein) results in over-diagnosis. It is desirable to avoid antimicrobials when their use is not indicated. Inappropriate use of antibiotics exposes the patient to the risk of unnecessary drug reactions and promotes development of resistant strains of bacteria.

It is essential to obtain urine cultures whenever antimicrobial therapy fails to ameliorate clinical signs or UTI recurs. Antimicrobial therapy should be withdrawn at least three days prior to collection of the urine sample for bacterial culture. Urine samples should ideally be cultured within 30 minutes after collection because multiplication or destruction of bacteria may be detected as early as one hour after urine collection. If immediate culture is not possible, urine may be stored refrigerated for up to six hours or in commercially available collection tubes containing preservatives for up to 72 hours.

Urine for culture should be obtained by cystocentesis whenever possible because this minimizes the risk of contaminating the sample. Nonetheless, even samples obtained by cystocentesis could be contaminated by skin bacteria, penetrating a loop of intestine, or on transfer of urine to culture media. If urine culture is obtained by means other than cystocentesis, differentiation between bacterial pathogens versus contaminants should be made based on results of quantitative urine cultures.

Diagnostic Evaluation - The Key to Successful Treatment of Recurrent UTI: Patients with recurrent UTI require additional diagnostic efforts because of the increased probability that conditions predisposing to or complicating infection are present. Therapy of UTI in these patients is most likely to succeed when these conditions are recognized and corrected. Initial patient evaluation should include a review of the medical history, physical examination, urinalysis, urine culture and susceptibility testing, renal function tests (serum urea nitrogen and/or creatinine concentrations), and survey abdominal radiographs. As described above, results of previous urine cultures make it possible to establish whether recurrence is due to relapse or reinfection. If initial tests confirm the diagnosis of bacterial UTI but fail to identify the cause or type of recurrence, consider recommending a four to six week course of antimicrobial therapy.

If infection recurs despite a properly performed course of antimicrobial therapy, further diagnostic efforts are indicated. Differentiating relapse from reinfection provides guidance in selecting appropriate diagnostic tests. Consider performing appropriate contrast radiographic or ultrasound procedures to rule-out urolithiasis, neoplasia, or structural abnormalities, or involvement of the upper urinary tract. Combined urography and double contrast cystography appears to be the most sensitive means of evaluating the lower urinary tract. Prostatic involvement may be investigated using ultrasound examination and cytology and culture of semen or prostatic biopsies. Intravenous urography and/or renal ultrasonography are indicated for evaluation of the upper urinary tract.

Definitive diagnosis of pyelonephritis is difficult. Only bacterial isolation from renal parenchyma or urine obtained from the renal pelvis provide conclusive proof of renal infection. Pyelonephritis may be suspected on the basis of clinical or laboratory findings suggesting renal involvement. Diagnosis of pyelonephritis may be supported by: 1) finding inflammatory casts on urinalysis, 2) obtaining a positive
bacterial culture from kidney or renal pelvis by fine needle aspiration, 3) renal biopsy and culture, 4) intravenous urography, or 5) renal ultrasonography.3

Hyperadrenocorticism and steroid therapy are relatively common yet overlooked causes for reinfections.4,5 Urinalysis findings of dogs with UTI associated with hyperadrenocorticism are often characterized by a lack of inflammatory reaction despite the presence of bacteriuria. Many affected dogs do not have clinical signs of urinary tract disease (asymptomatic bacteriuria).

Management Guidelines: Patients with recurrent UTI are often managed by repeated attempts at antimicrobial therapy using the same or different antibiotics. Unfortunately, this approach frequently fails because it does not address the causes responsible for therapeutic failure. While the initial diagnosis of UTI is often based on clinical findings and urinalysis results, the diagnosis of bacterial UTI should be confirmed whenever antimicrobial therapy fails to ameliorate clinical signs or UTI recurs.

Antimicrobial Selection: Susceptibility testing should be performed on all urinary bacterial isolates from patients with recurrent UTI. However, it is important to remember that as a result of renal excretion, many antimicrobial agents attain substantially higher concentrations in urine than in blood. The drug selected should be administered frequently enough to maintain inhibitory concentrations in urine and for sufficient time to eliminate the infecting agent from the urinary tract.

Recognition of renal or prostatic involvement is an important factor in formulating therapeutic plans for patients with recurrent UTI. Decisions concerning treatment for superficial infections of the lower urinary tract urothelium can be based on urine antimicrobial concentrations. However, it is necessary to select antimicrobial agents that attain high concentrations in serum and urine to eradicate deep seated infections such as pyelonephritis or prostatitis. Fluoroquinolones are the antimicrobial agents most likely to achieve therapeutic concentrations in renal tissue in patients with pyelonephritis. Because of the blood prostatic fluid barrier is expected to be intact in chronic prostatitis, an appropriate antimicrobial which will attain therapeutic concentrations in prostatic secretions should be selected (e.g. quinolones, trimethoprim-sulfonamide combinations, chloramphenicol, clindamycin, erythromycin, or oleandomycin).

Protocol for Therapy and Follow-up of Recurrent UTI: Therapy is successful only if the urine does not contain any pathogenic organisms. Treatment is ineffective and relapse will occur if the bacterial colony count has only been reduced. Culture a urine sample collected by cystocentesis three to five days following initiation of antimicrobial therapy. Performing urine culture at this time is designed to recognize treatment failure so that a prolonged period of unnecessary and expensive antimicrobial therapy can be avoided. If bacterial growth is detected 3 to 5 days after initiating therapy, treatment should be reevaluated. If the urine is sterile 3 to 5 days after initiating therapy, treatment should be continued.

Data concerning the minimum and optimum duration of antimicrobial therapy for UTIs are not available. It is recommended that acute, uncomplicated UTIs and some reinfections be treated for a period of 10 to 14 days whereas chronic or persistent UTI should be treated for at least 4 to 6 weeks. Some infections involving the kidney(s) and prostatic gland may require even more prolonged therapy. The client should be informed that amelioration of clinical signs is not a reliable indicator of successful eradication of UTI, and medication should be administered throughout the recommended treatment interval. To ensure adequate concentrations of drug remain in the urinary tract, it is recommended that daily doses be administered after micturition and particularly before periods of confinement.

Urine may be cultured immediately before discontinuing therapy to ensure that infection has been eradicated and superinfection has not developed. Bacterial culture should then be performed on urine obtained by cystocentesis 7 to 10 days after completing therapy to detect relapses. Urine should also be cultured approximately 1, 2, 3, 6, and 12 months after terminating therapy to detect reinfections or delayed relapses.

Prophylactic Therapy: When reinfection occurs four or more times in a year and predisposing causes of UTI cannot be identified or eliminated, or their apparent elimination does not prevent recurrence, long-term, low-dose antimicrobial therapy may be necessary to prevent reinfection. Before initiating long-term antimicrobial therapy, urine should be sterile. Antimicrobial drugs should be administered nightly after micturition and before bedtime for at least 6 months. Administration before bedtime (or other extended interval of confinement) assures that the urinary bladder fills with urine containing a high concentration of the antimicrobial agent. During long-term therapy, the effectiveness of prophylactic therapy should be confirmed by urine cultures performed by cystocentesis about every 4 to 6 weeks. If urine cultures are negative, therapy is continued. Many patients which remain uninfected for 6 months do not develop additional episodes of infection. However, long-term, low-dose antimicrobial therapy may be continued for extended periods (even years) in patients that continue to experience frequent reinfections.

References