U - Nephrology & Urology
URINARY TRACT INFECTION

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ETIOLOGY

Urinary tract infection (UTI) encompasses a wide variety of clinical entities caused by microbial invasion of any part of the urinary system. Infection induces inflammation of the urethra (urethritis), prostate gland (prostatitis), bladder (cystitis), ureters (ureteritis), and kidneys (pyelonephritis).

Hematogenous renal infection such as septic infarcts from bacterial endocarditis can induce acute renal failure. However, the hematogenous route is not a common mechanism for establishment of UTI in dogs and cats. Most UTI is caused by bacteria emanating from the gastrointestinal tract crossing the perineum and colonizing the external genitalia prior to retrograde invasion of the urethra and bladder against the flow of urine. Further ascending colonization of the ureters and kidneys can occur but this is relatively uncommon. Development of UTI depends upon the balance between infectious agents and host resistance, and the status of host defense mechanisms appears to be important in the pathogenesis of UTI. Although UTI can occur when a very virulent organism invades a normal urinary tract, many times UTI develops when there is a disturbance of anatomical or functional factors that normally prevent microbial invasion.

The recognized etiological agents involved in UTI are mainly bacteria (Table 1). However, fungi can colonize the urinary tract in special circumstances. The role of viruses in UTI is currently not known.

Table 1: Bacterial isolates in canine UTI

	Per cent of total isolates		
	a)	(b)	(c)
E. coli	37.8	67	20.1
Staphylococcus spp.	14.5	21	9.6
Proteus mirabilis	12.4	3	15.4
Streptococcus spp.	10.7	6	10.6
Klebsiella pneumoniae	8.1	0	3.4
Pseudomonas aeruginosa	3.4	0	6.9
Enterobacter spp.	2.6	3	3.3
Number of isolates:	1,400	40	187

(a) Ling, G.V. et al. Vet. Clin. North Amer. 1979; 9: 617-630
(b) Kivisto, A.K. et al. J. Sm. Anim. Pract. 1997; 18: 707-712
(c) Wooley RE et al. Mod Vet Pract. 1976; 57: 535-538.

Whether or not UTI develops depends on a balance between virulent bacteria that tend to ascend the urinary tract and natural host defenses that tend to keep them out.

Host defense mechanisms

Many host defense mechanisms have been identified or hypothesized to be important in protection against UTI (Table 2).

Table 2: Local host defenses of the urinary tract

- Normal Micturition
  - Adequate urine flow
  - Frequent voiding
  - Complete voiding
- Anatomic Structures
  - Urethral high pressure zone
  - Surface characteristics of urethral urothelium
  - Urethral peristalsis
  - Prostatic antibacterial fraction
  - Length of urethra
  - Ureterovesical flap valves and ureteral peristalsis
- Mucosal Defense Barriers
  - Antibody production
  - Surface glycosaminoglycan layer
  - Intrinsic mucosal antimicrobial properties
  - Bacterial interference
  - Exfoliation of cells
- Antimicrobial Properties of Urine
  - Extremes (high or low) of urine pH
  - Hyperosmolality
  - High concentration of urea
  - Organic acids
- Renal Defenses
  - Glomerular mesangial cells?
  - Extensive blood supply and large blood flow

Bacterial virulence

Of all the bacterial species resident in the gastrointestinal tract only a few are capable of causing UTI. In order to be successful uropathogens, bacteria must possess special properties that enable them to invade and persist in the urinary tract. The intrinsic motility of some bacteria may aid in their retrograde migration through the excretory pathway against the flow of urine. The ability to adhere to the surface of uroepithelial cells is very important because it prevents urine flow from washing bacteria out and it allows more efficient delivery of bacterial toxins to the mucosal wall.

The consequences of UTI are variable. In many cases, infection will be transient, signs will be minimal, and the condition responds readily to treatment. However, UTI is often subclinical and goes undetected for long periods. Many infections can persist for a prolonged period in a commensal-like relationship with the host animal causing few if any detrimental effects. However, serious consequences of persistent UTI include formation of struvite uroliths, chronic prostatitis, prostatic abscess formation, discospondylitis and ascending renal infection with scarring, progressive loss of renal function and chronic renal failure. Whether an infection will be benign or injurious cannot be predicted, so all UTI should be treated vigorously.

DIAGNOSIS

In animals that exhibit overt clinical signs of lower urinary tract inflammation, the major diagnostic possibilities include UTI, urolithiasis and lower urinary tract neoplasia. Bladder and urethral neoplasia is rare in dogs under 7 years of age. Clinicians should always remember that UTI could coexist with both urolithiasis and neoplasia.

The diagnosis of UTI is often made on clinical history and physical examination alone. However, a more definitive approach with urinalysis, urine culture, and antimicrobial sensitivity testing is recommended, particularly if previous treatment has been unsuccessful. The interpretation of urinalysis and bacterial culture results depends upon the method of collection. Urine collected by mid-stream voiding, catheterization and cystocentesis can all be useful but cystocentesis urine is best for culture.

Urine should be set up for bacterial culture as soon as possible after collection and certainly no longer than 4 hours.

Antimicrobial sensitivity tests

Antimicrobial sensitivity tests on uropathogens are best performed using the minimum inhibitory concentration (MIC) method. The mean urinary concentration (MUC) achieved with standard dose regimens has been determined for most of the antimicrobial agents used to treat UTI. If an antimicrobial reaches an MUC of at least 4 times the *in vitro* MIC, treatment with that drug has a high chance of therapeutic success.

The MUC in dogs of commonly used antimicrobials when given at usual recommended doses can be obtained by contacting the author.

Localization of infection

Clinically it is difficult to determine if UTI is confined to the lower urinary tract or has extended to involve the kidneys. Animals with pyelonephritis can have WBC casts in the urine sediment, dilute urine, and peripheral leukocytosis. About 90 % of intact male dogs with UTI have colonization of the prostate.

TREATMENT

Several bacteria commonly isolated from UTI in dogs and cats have predictable antimicrobial sensitivity and their presence can be deduced from a urinalysis. If cocci are observed in the urine sediment (*Staphylococcus intermedius, Streptococcus* spp., and *Enterococcus* spp.) or the urine is very alkaline and small rods in pairs are evident in the urine sediment (*Proteus mirabilis*), over 90 % will be sensitive to ampicillin or amoxicillin. Combination with the β–lactamase

inhibitor clavulanic acid may be preferable.
Other bacteria causing UTI must be identified by culture. Fluoroquinolones are very effective in the treatment of *Pseudomonas aeruginosa* and for lower urinary tract infections in female dogs, tetracyline may be quite effective as well. The antimicrobial sensitivities of *E. coli, Klebsiella* spp. and *Enterobacter* spp. are not predictable and sensitivity tests must be performed to determine appropriate treatment.

Duration of treatment

The accepted duration of treatment for UTI of the lower urinary tract is 14 days. Treatment duration of up to 30 days is usually recommended for patients where the infection is suspected to involve prostatic or renal tissue.
A urine culture should be performed 8-10 days after beginning treatment to ensure that the chosen antimicrobial is effective. Another urine culture should be performed 10 days after cessation of treatment to ensure that treatment has been successful and persistent or recurrent UTI is not present.

Special considerations

For intact male dogs with UTI, antimicrobial agents must be weak bases or at least lipid soluble and they must achieve a plasma concentration of 4 times MIC. Fluoroquinolones (broad spectrum weak bases), trimethoprim (a weak base), and chloramphenicol (lipid soluble) are all suitable for male dogs with prostatic involvement.
Occasionally fungal and yeast overgrowth will colonize the urinary tract, particularly in patients with diabetes mellitus. Elimination of the underlying cause usually is sufficient to clear the infection. Amphotericin B used as a local irrigant into the bladder has been suggested for persistent infections. Fluconazole and ketoconazole have been used successfully to treat fungal cystitis in humans but information is lacking in veterinary medicine. Mild alkalinization of the urine is also thought to be helpful.

Treatment failure

Failure of an antimicrobial agent to sterilize the urine should alert the clinician to one or more of the following possibilities:

1. Inappropriate drug, dose, or duration of therapy.
2. Failure of the antimicrobial agent to reach sufficient concentrations in urine.
3. The presence of a nidus of infection
4. The presence of anatomical or functional abnormalities.

When UTI recurs after apparently effective treatment has been given for a reasonable period of time, in male dogs a routine work up for prostatic disease should be performed including ultrasonic examination of the prostate and cytology and culture of a prostatic aspirate. Plain and contrast radiographic studies including IVP, double contrast cystography and retrograde and voiding urethrography should be sufficient to diagnose or rule out the presence of identifiable anatomical defects. Urolithiasis is a frequent cause of recurrent lower urinary tract inflammation in animals of all ages, while neoplasia of the bladder, urethra or prostate can be the underlying problem in older dogs.

PREVENTION

When an animal suffers frequent recurrences of UTI despite adequate treatment and in the absence of detectable or correctable anatomic and functional disturbances, long term management with antimicrobial agents may be necessary to prevent additional recurrences. Patients must first be given a standard treatment of antimicrobial based on sensitivity results for 14 or 30 days, as required. Then, the protocol calls for continued administration of an antimicrobial at 30-50 % of the usual total daily dose given as a single dose at night before bedtime immediately after the animal is allowed to void. Treatment should be given for 6 months.

REFERENCES

Available on request