Urinary Tract Infections
Treatment/Comparative Therapeutics

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INTRODUCTION
Urinary tract infection (UTI) occurs when there is a compromise of host defense mechanisms and a virulent microbe adheres, multiplies, and persists in a portion of the urinary tract. Host defenses include normal micturition, anatomic structures, the mucosal barrier, properties of urine, and systemic immunocompetence. Most commonly UTIs are caused by bacteria, but fungi and viruses also may infect the urinary tract. UTIs may involve more than one anatomic location, and the infection should be categorized as upper urinary tract (kidneys and ureters) versus lower urinary tract (bladder, urethra, and vagina). Most bacterial UTI occur as a consequence of ascending migration of pathogens through the genital tract and urethra to the bladder, ureters, and one or both kidneys. Rectal, perineal, and genital bacteria serve as the principal reservoirs for infection.1,2

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**Bacterial Isolates**

A single bacterial pathogen is isolated from approximately 75% infections; 20% of UTIs are caused by 2 coinfecting species, and approximately 5% are caused by 3 species.\(^3\)\(^-\)\(^5\)

The bacteria that most commonly cause UTIs are similar in dogs and cats (Fig. 1).\(^3\)\(^-\)\(^8\) *Escherichia coli* is most common, followed by gram-positive cocci, and then various others, including *Proteus*, *Klebsiella*, *Pasteurella*, *Pseudomonas*, *Corynebacterium*, and several other rarely reported genera.\(^3\)\(^,\)\(^6\)\(^-\)\(^8\) *Mycoplasma* spp are isolated from urine of dogs with clinical signs of lower urinary tract in less than 5% of samples; whether *Mycoplasma* spp are associated with urinary tract disease in cats is controversial.\(^3\)\(^,\)\(^9\)\(^-\)\(^11\)

Cats may be infected with a unique strain of *Staphylococcus*, *Staphylococcus felis*, and commercial phenotypic identification systems may not differentiate between *S. felis* and other coagulase-negative *Staphylococcus* spp.\(^7\)\(^,\)\(^8\) One study found that *S. felis* was the third most common isolate based on 16S rDNA sequencing (n = 25/106, 19.8% of bacterial isolates cultured), suggesting *S. felis* is the most common *Staphylococcal* species causing UTI in cats.\(^7\)

**Pyelonephritis**

Pyelonephritis, or infection of the renal pelvis and parenchyma, is most commonly due to ascending infections from the lower urinary tract in dogs and cats (Fig. 2). In addition to the components of immunity that protect urinary tract in general, the kidneys are protected from bacterial infection by vesicoureteral flap valves, relatively long ureters that usually allow only one-way flow of urine via peristalsis, and generally hypoxic environment of the renal medulla.

**Prostatitis**

Inherent prostatic defense mechanisms against infection include local immune factors, such as immunoglobulin A and antibacterial proteins, retrograde flow of prostatic
fluid and urine, and urethral peristalsis, and the urethral high pressure zone.\textsuperscript{12,13} Dogs with bacterial prostatitis often have alteration of normal defenses, such as underlying benign prostatic hyperplasia, prostatic cysts, or neoplasia.\textsuperscript{14} Most commonly prostatitis develops from ascending bacterial infection and may result in prostatic abscessation in addition to prostatic parenchymal infection (Fig. 3). Hematogenous spread and prostatitis secondary to cystitis are also possible. Bacterial pathogens are similar to those causing bacterial cystitis with \textit{E coli} being the most common (see Fig. 1). \textit{Brucella canis} should also be considered, especially for intact male dogs, as a cause for both acute and chronic prostatitis.\textsuperscript{14}

\textbf{Catheter-associated urinary tract infection}

Normal host defense mechanisms are effective in preventing bacterial UTIs; however, they are not impenetrable. Normal host defenses may be overwhelmed if large quantities of a virulent uropathogen are introduced into the urinary tract during diagnostic and therapeutic procedures. Catheter-associated bacterial UTI is a common complication of indwelling urinary catheters, especially if an open-ended system is used. In a

\textbf{Fig. 3.} (A) Sagittal ultrasonographic image of the prostate and urinary bladder showing 2 cystic lesions that were abscesses (*) and (B) purulent prostatic wash fluid due to \textit{E coli} in a 6-year-old intact male Rhodesian ridgeback.
clinical study, infection developed in 30% to 52% of dogs and cats with indwelling urinary catheters; risk of infection increased with duration of catheterization. The risk of infection is further compounded if the patient has pre-existing urinary tract disease. Use of indwelling urinary catheters during diuresis or corticosteroid administration is particularly dangerous.

**Fungal Urinary Tract Infection**

Fungal UTI is uncommon. As with bacterial UTI, fungal UTI occurs because of temporary or permanent breaches in local or systemic immunity of the lower urinary tract. Funguria may be due to primary infections of the lower urinary tract or secondary to shedding of fungal elements into the urine in animals with systemic infections. Primary fungal UTI is most commonly due to *Candida* spp, a commensal inhabitant of the genital mucosa, upper respiratory tract, and gastrointestinal tract. *Candida albicans* is the most commonly identified species, followed by *Candida glabrata* and *Candida tropicalis*; other ubiquitous fungi may also occasionally cause primary fungal UTI, including *Aspergillus* spp, *Blastomyces* spp (Fig. 4), and *Cryptococcus* spp.

**Viral Urinary Tract Infection**

Viral-induced disease in humans is increasingly recognized, especially of the upper urinary tract. However, it can be difficult to determine cause-and-effect relationships because viral-induced disease may occur in the absence of detectable replicating virus. Several viruses have been implicated in canine and feline disease (Box 1).

**PATIENT EVALUATION OVERVIEW**

**Clinical Signs**

*Lower urinary tract infection: bacterial, fungal, viral*

Lower UTI may be symptomatic or asymptomatic, and clinical signs are indistinguishable from other causes of lower urinary tract disease. Nonspecific clinical signs of lower urinary tract disease include, but are not limited to, pollakiuria, dysuria, stranguria, hematuria, and inappropriate urination.

**Prostatitis** Acute prostatitis is usually associated with systemic illness, including fever, anorexia, vomiting, and lethargy. Dogs with acute disease may also have caudal abdominal pain, stiff gait, and preputial discharge and be unwilling to breed. In contrast, dogs with chronic prostatitis are usually not systemically ill or febrile.
Commonly, recurrent UTI or preputial bloody discharge is the only clinical sign of chronic prostatitis. Other presentations include stiff gait, discomfort with rising, infertility, or orchiepididymitis, or dogs may be asymptomatic.

**Upper urinary tract infection**

**Pyelonephritis** Pyelonephritis may have an acute or chronic presentation. Acute pyelonephritis is usually associated with signs of severe systemic illness (e.g., uremia, fever, painful kidneys, possible nephromegaly, and/or sepsis). In contrast, chronic pyelonephritis usually has a more insidious presentation: slowly progressive azotemia that may not be associated with uremia, progressive kidney damage, and ultimately, renal failure if untreated. Bacterial pyelonephritis may be associated with hematuria only.

**Diagnosis**

**Bacterial urinary tract infection**

In addition to clinical signs, results of a complete urinalysis may provide evidence of a bacterial UTI. Hematuria, pyuria, and bacteriuria are often present unless there is suppression of immune response because of underlying disease or drugs (Fig. 5).

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**Box 1**

**Viruses associated with urinary tract disease in dogs and cats**

| Species   | Upper Urinary Tract Disease                  | Lower Urinary Tract Disease         |
|-----------|---------------------------------------------|------------------------------------|
| Canine    | Canine adenovirus type I                    |                                    |
|           | Canine herpesvirus                          |                                    |
| Feline    | Feline coronavirus                          | Feline calicivirus                  |
|           | Feline immunodeficiency virus               | Bovine herpesvirus-4                |
|           | Feline leukemia virus                       |                                    |
|           | Feline foamy (syncytium-forming) virus      | Feline foamy (syncytium-forming) virus |

Adapted from Kruger JM, Osborne CA, Wise AG, et al. Viruses and urinary tract disease. In: Polzin D, Bartges JW, editors. Nephrology and urology of small animals. Chichester (United Kingdom): Blackwell Publishing Ltd; 2011. p. 725–33.

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Fig. 5. Microscopic examination of a modified Wright stain urine sediment from a dog with *E coli* bacterial cystitis showing white blood cells and bacteria (×400).
Microscopic examination of unstained urine sediment is less sensitive and specific than examining urine sediment stained with a modified Wright stain. A positive urine culture is the “gold standard” for diagnosing bacterial UTI. A quantitative urine culture includes isolation and identification of the organism and determination of the number of bacteria (colony-forming units per unit volume). Quantitation of bacteria enables interpretation as to the significance of bacteria present in a urine sample. Caution should be exercised when interpreting quantitative urine cultures obtained by midstream voiding or manual expression of urine.

Determining whether an infection is uncomplicated or complicated is essential to guide the diagnostic and therapeutic plan. A simple uncomplicated UTI occurs sporadically in an otherwise healthy animal with a normal structural and functional urinary tract. In contrast, infections are complicated if there is (1) involvement of the upper urinary tract and/or prostate, (2) an underlying comorbidity that alters the structure or function of the urinary tract, such as an endocrinopathy or chronic kidney disease (CKD), or (3) recurrent infection. Recurrent infections are further categorized as relapsing, refractory/persistent, reinfection, or superinfection (Table 1). Most cats with bacterial UTI have complicated infections. Additional laboratory testing and imaging studies are often required for complicated infections (Box 2).

Pyelonephritis Pyelonephritis is an example of a complicated UTI. Diagnosis of pyelonephritis is usually presumptive based on positive urine culture, concurrent consistent renal diagnostic imaging abnormalities (eg, pyelectasia), and possible improvement in degree of azotemia following antimicrobial therapy. Although a positive culture is helpful for the diagnosis, a negative urine culture does not rule out pyelonephritis.

Prostatitis All dogs with suspected prostatic disease should have a complete physical examination, including rectal examination, and a minimum database with complete blood count, chemistry panel, urine analysis, and urine culture. Abdominal radiographs and ultrasound are useful to determine the size, shape, location, and architecture of the prostate as well as if any cysts or abscesses are present (see Fig. 3A). Prostatic fluid should be evaluated for cytology and bacterial culture and sensitivity (see Fig. 3B). Options for prostatic fluid sampling are discussed elsewhere, but include semen evaluation of the third fraction, prostatic wash, fine-needle aspiration, and prostatic biopsy.

Catheter-associated urinary tract infection There is no evidence to support routine urine culture or culture of the urinary catheter tip following removal in asymptomatic patients; such cultures do not predict the development of catheter-associated infection. In contrast, urine culture is always indicated for a patient with clinical signs of UTI, fever of undetermined origin, or abnormal urine cytology (ie, hematuria, pyuria). If the patient develops new clinical signs or fever after a urinary catheter has been placed, then, ideally, the urine catheter is removed and a cystocentesis is performed to provide a sample for culture once the bladder fills. Alternatively, the original urinary catheter is replaced and a urine sample is collected through the second catheter. It is less ideal to sample the urine through the original catheter, and a sample from the collection bag should never be used.

Asymptomatic bacteriuria Asymptomatic bacteriuria (AB) is a common and often benign finding in healthy women. Risk factors include pregnancy, diabetes mellitus, spinal cord injury, indwelling urinary catheter, and being an elderly nursing home resident. Women with AB have more frequent symptomatic episodes, but antimicrobial treatment does not decrease the number of episodes. A benefit to treatment has not
| Table 1 | Uncomplicated and complicated urinary tract infections |
|---------|-------------------------------------------------------|
| **Definition** | **Underlying Cause** |
| Uncomplicated UTI | Healthy individual, normal urinary tract anatomy and function | Sporadic infection |
| Complicated UTI | Disease that alters the structure or function of the urinary tract | Endocrinopathies  
- Diabetes mellitus  
- Hyperadrenocorticism  
- Hyperthyroidism  
- CKD  
- Urinary or reproductive tract anatomic abnormality  
- Immunocompromised  
- Neurogenic bladder  
- Pregnancy |
| Comorbidity | Relevant comorbidity predisposes to persistent infection, recurrent infection, or treatment failure |
| Recurrent infection | Recurrence within weeks to months of a successfully treated infection | Failure to eradicate pathogen  
- Deep-seated niche  
- Pyelonephritis  
- Prostatitis  
- Bladder submucosa  
- Stone  
- Neoplasia |
| Relapsing | Sterile bladder during treatment  
- Same organism |
| Refractory/persistent | Persistently positive culture with original pathogen despite in vitro antimicrobial susceptibility  
- No elimination of bacteriuria during or after treatment |
| Reinflection | Recurrence with different organism  
- Variable time course after previous infection |
| Superinfection | Infection with different pathogen during treatment of the original infection |

Adapted from Weese JS, Blondeau JM, Boothe D, et al. Antimicrobial use guidelines for treatment of urinary tract disease in dogs and cats: antimicrobial guidelines working group of the international society for companion animal infectious diseases. Vet Med Int 2011;2011:1–9; and Barsanti J. Multidrug-resistant urinary tract infection. In: Bonagura JD, Twedt DC, editors. Current veterinary therapy XIV. St Louis (MO): WB Saunders; 2009. p. 921–5.
been found with clinical trials in humans, whereas potential complications include adverse drug reactions and the development of antimicrobial resistance.\textsuperscript{25}

The prevalence of AB in healthy dogs and cats is low (2\%-9\%).\textsuperscript{26–29} Animals with underlying comorbidities, such as hyperthyroidism, diabetes mellitus, or CKD, or recurrent infection have increased prevalence of AB, up to 30\%\textsuperscript{29–33} and 50\%,\textsuperscript{34} respectively. There are no prospective studies comparing clinical outcome in veterinary patients with or without antimicrobial treatment of AB. In one recent prospective study of dogs with AB, 50\% had transient colonization and 50\% had persistent bacteriuria over a 3-month time period; no dog developed clinical signs at any time point.\textsuperscript{27} Similar to general recommendation in humans, treatment is not recommended for AB unless there is a high risk for ascending or systemic infection (eg, immunocompromised patients, CKD).\textsuperscript{23}

\textbf{Fungal urinary tract infection}

Diagnosis of fungal UTI most commonly occurs by identification of fungal elements during routine or concentrated urine sediment examination. Fungal culture and

\begin{table}[h]
\centering
\begin{tabular}{|l|}
\hline
\textbf{Box 2} \\
Diagnostic testing for complicated urinary tract infections \\
\hline
\textit{Extended diagnostic testing may be required for complicated infections.}
\begin{itemize}
\item Urine analysis
\item Urine culture (ideally, cystocentesis sample)
\item Complete blood count
\item Chemistry profile with electrolytes
\item Digital rectal examination
\item Feline leukemia virus/feline immunodeficiency virus (cats)
\item Thyroid testing
  \begin{itemize}
  \item Cats: total T4
  \end{itemize}
\item Adrenal testing
  \begin{itemize}
  \item Low-dose dexamethasone suppression test
  \item Adrenocorticotrophic hormone stimulation test
  \end{itemize}
\item Abdominal radiographs
\item Abdominal ultrasound
\item Contrast radiology
  \begin{itemize}
  \item Excretory urography
  \item Contrast cystourethrography
  \item Double-contrast cystography
  \item Contrast vaginourethrography
  \end{itemize}
\item Prostatic wash
\item Cystoscopy with bladder wall culture
\end{itemize}
\end{tabular}
\caption{Diagnostic testing for complicated urinary tract infections}
\end{table}

\textit{Adapted from} Bartges JW. Diagnosis of urinary tract infections. Vet Clin North Am Small Anim Pract 2004;34:927–29; and Weese JS, Blondeau JM, Boothe D, et al. Antimicrobial use guidelines for treatment of urinary tract disease in dogs and cats: antimicrobial guidelines working group of the international society for companion animal infectious diseases. Vet Med Int 2011;2011:2,4.
sensitivity are ideal before treatment, especially in cases other than *C. albicans*, which tend to be more resistant. 19

**Viral urinary tract infection**
Routine diagnostic tests, including urine analysis and light microscopy, cannot identify viruses or viral-induced disease. Virus isolation is the gold standard for diagnosis, but this technique is expensive and time-consuming and requires live replicating virus. Diagnostic polymerase chain reaction assays are rapid and sensitive, but methods to optimize nucleic acid preparation are essential because the nucleic acids are easily degraded in urine. 20

**PHARMACOLOGIC TREATMENT OPTIONS**

**Antimicrobials**
Antimicrobial drugs are the cornerstone of treatment of UTI. In most cases the antimicrobial agent chosen should be based on susceptibility testing of the uropathogen. Overuse and misuse of antimicrobial drugs may result in the emergence of resistant organisms, a situation that has implications for successful treatment of infections in the patient as well as overall veterinary and human health.

Patients with uncomplicated UTI and those with clinical signs severe enough to merit therapy before results of urine culture and sensitivity testing should receive a broad-spectrum antimicrobial that has excellent urine penetration. Suggested “first-line” antimicrobials for uncomplicated UTIs include amoxicillin, cephalexin, or trimethoprim-sulfamethoxazole (Table 2). The use of potentiated β-lactams (ie, amoxicillin-clavulanic acid), fluoroquinolones, or extended-release cephalexin (ie, cefovecin) is inappropriate for most uncomplicated UTIs and should be reserved for complicated or resistant infections (Table 3).

**Combination therapies**
If multiple bacteria are isolated, then the relative importance of each must be assessed based on quantification and suspected pathogenicity. Ideally, an antimicrobial effective against all pathogens is selected. If this is not possible, then combination therapy with multiple antimicrobials may be considered. 23 Assuming there is no evidence of pyelonephritis or increased risk of ascending infection, then targeting antimicrobial therapy against the pathogen with most clinical relevance is reasonable. For example,

| Infection                  | First-Line Drug Options                                    |
|----------------------------|-----------------------------------------------------------|
| Uncomplicated UTI          | Amoxicillin, trimethoprim-sulfamethoxazole                 |
| Complicated                | Guided by culture and susceptibility testing, but consider amoxicillin or trimethoprim-sulfamethoxazole initially |
| Subclinical bacteriuria    | Antimicrobial therapy not recommended unless high risk for ascending infection. If so, treat as per complicated UTI |
| Pyelonephritis             | Start with a fluoroquinolone, with reassessment based on culture and susceptibility testing |
| Prostatitis                | Trimethoprim-sulfamethoxazole, enrofloxacin, chloramphenicol |

*Adapted from* Weese JS, Blondeau JM, Boothe D, et al. Antimicrobial use guidelines for treatment of urinary tract disease in dogs and cats: antimicrobial guidelines working group of the International Society for Companion Animal Infectious Diseases. Vet Med Int 2011;2011:5,6.
| Drug               | Dose                                      | Comments                                                                                                                                                                                                 |
|--------------------|-------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Amoxicillin        | 11–15 mg/kg q8h, PO                       | Good first-line option for UTIs. Excreted in urine predominantly in active form if normal renal function is present. Ineffective against β-lactamase-producing bacteria.                                    |
| Amikacin           | Dogs: 15–30 mg/kg q24h, IV/IM/SC          | Not recommended for routine use but may be useful for treatment of multidrug-resistant organisms. Potentially nephrotoxic. Avoid in animals with renal insufficiency.                                           |
|                    | Cats: 10–14 mg/kg q24h, IV/IM/SC          |                                                                                                                                                                                                       |
| Amoxicillin/clavulanate | 12.5–25 mg/kg q8h, PO (dose based on combination of amoxicillin + clavulanate) | Not established whether there is any advantage over amoxicillin alone.                                                                                                                                 |
| Ampicillin         |                                            | Not recommended because of poor oral bioavailability. Amoxicillin is preferred.                                                                                                                                                      |
| Cephalexin, Cefadroxil | 12–25 mg/kg q12h, PO                       | Enterococci are resistant. Resistance may be common in Enterobacteriaceae in some regions                                                                                                                                          |
| Cefovecin          | 8 mg/kg single SC injection. Can be repeated once after 7–14 d | Should only be used in situations where oral treatment is problematic. Enterococci are resistant. Pharmacokinetic data are available to support the use in dogs and cats, with a duration of 14 d (dogs) and 21 d (cats). The long duration of excretion in the urine makes it difficult to interpret posttreatment culture results. |
| Cefpodoxime proxetil | 5 to 10 mg/kg q24h, PO                     | Enterococci are resistant.                                                                                                                                                                                                                      |
| Ceftiofur          | 2 mg/kg q12–24h, SC                       | Approved for treatment of UTIs in dogs in some regions. Enterococci are resistant.                                                                                                                                                      |
| Chloramphenicol    | Dogs: 40–50 mg/kg q8h, PO                 | Reserved for multidrug-resistant infections with few other options. Myelosuppression can occur, particularly with long-term therapy. Avoid contact by humans because of rare idiosyncratic aplastic anemia.               |
|                    | Cats: 12.5–20 mg/kg q12h, PO              |                                                                                                                                                                                                       |
| Ciprofloxacin      | 30 mg/kg q24h, PO                         | Sometimes used because of lower cost than enrofloxacin. Lower and more variable oral bioavailability than enrofloxacin, marbofloxacin, and orbifloxacin. Difficult to justify over approved fluoroquinolones. Dosing recommendations are empirical. |
| Doxycycline        | 3–5 mg/kg q12h, PO                        | Highly metabolized and excreted through intestinal tract, so urine levels may be low. Not recommended for routine uses.                                                                                                                     |
| Antimicrobial          | Dosing & Notes                                                                                                                                                                                                                                                                                                                                 |
|-----------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Enrofloxacin          | **Dogs:** 10–20 mg/kg q24h, PO  
**Cats:** 5 mg/kg q24h, PO  
Excreted in urine predominantly in active form. Reserve for documented resistant UTIs but good first-line choice for pyelonephritis (dogs 20 mg/kg PO q24h). Limited efficacy against enterococci. Associated with risk of retinopathy in cats. Do not exceed 5 mg/kg/d of enrofloxacin in cats. |
| Imipenem-cilastatin   | 5 mg/kg q6–8h, IV/IM  
Reserve for treatment of multidrug-resistant infections, particularly those caused by *Enterobacteriaceae* or *P. aeruginosa*. Recommend consultation with a urinary or infectious disease veterinary specialist or veterinary pharmacologist before use.                                                                                     |
| Marbofloxacin         | 2.7–5.5 mg/kg q24h, PO  
Excreted in urine predominantly in active form. Reserve for documented resistant UTIs but good first-line choice for pyelonephritis. Limited efficacy against enterococci.                                                                                                                  |
| Meropenem             | 8.5 mg/kg q12h, SC or q8h, IV  
Reserve for treatment of multidrug-resistant infections, particularly those caused by *Enterobacteriaceae* or *P. aeruginosa*. Recommend consultation with a urinary or infectious disease veterinary specialist or veterinary pharmacologist before use.                                                                 |
| Nitrofurantoin        | 4.4–5 mg/kg q8h, PO  
Good second-line option for simple uncomplicated UTI, particularly when multidrug-resistant pathogens are involved.                                                                                                                                                                                                                       |
| Orbifloxacin          | Tablets: 2.5–7.5 mg/kg q24h, PO; oral suspension: 7.5 mg/kg q24h, PO (cats) or 2.5–7.5 mg/kg q24h, PO (dogs)  
Excreted in urine predominantly in active form.                                                                                                                                                                                                                                          |
| Pradofloxacin         | **Dogs:** 3 mg/kg q24h, PO  
**Cats:** 5 mg/kg q24h, PO  
May cause bone marrow suppression resulting in severe thrombocytopenia and neutropenia in dogs.                                                                                                                                                                                                                         |
| Trimethoprim-sulfadiazine | 15 mg/kg q12h, PO  
Note: dosing is based on total trimethoprim + sulfadiazine concentration  
Good first-line option. Concerns regarding idiosyncratic and immune-mediated adverse effects in some patients, especially with prolonged therapy. If prolonged (>7 d) therapy is anticipated, baseline Schirmer tear testing is recommended (dogs), with periodic re-evaluation and owner monitoring for ocular discharge. Avoid in dogs that may be sensitive to potential adverse effects such as keratoconjunctivitis sicca (KCS), hepatopathy, hypersensitivity, and skin eruptions. |

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*a Dose extrapolated from previous studies.*

*Adapted from Weese JS, Blondeau JM, Boothe D, et al. Antimicrobial use guidelines for treatment of urinary tract disease in dogs and cats: antimicrobial guidelines working group of the International Society for Companion Animal Infectious Diseases. Vet Med Int 2011;2011:5,6.*
anecdotally, resolution of *Enterococcus* sp infection is often possible after treatment of concurrent infection.\(^{23}\)

**Fluoroquinolone update**

The use of fluoroquinolones for empiric treatment of bacterial UTI is discouraged because of the inherent resistance of many gram-positive organisms to this class of antimicrobials, and the developing resistance of many gram-negative organisms, including *E coli*, to this class of drugs.\(^ {35}\) Studies have found variable cross-resistance among different generations of fluoroquinolones, except pradofloxacin (Veraflox), and once fluoroquinolone resistance has developed, a later generation of drug may not be beneficial.\(^ {36}\) In vitro, pradofloxacin, a third-generation fluoroquinolone, outperformed other fluoroquinolones in terms of potency and efficacy; enrofloxacin was the least potent second only to ciprofloxacin. Molecular alterations of pradofloxacin allow increased bactericidal activity and decreased propensity for antimicrobial resistance.\(^ {35-37}\) These features make pradofloxacin an attractive choice for a susceptible fluoroquinolone-naïve isolate or pathogens with reduced fluoroquinolone susceptibility.\(^ {36,38}\) Currently, pradofloxacin is only licensed for feline skin infections in the United States, whereas the European license includes a wide range of indications for both dogs and cats. One prospective clinical trial (n = 78) found pradofloxacin was effective and well-tolerated for feline bacterial UTI.\(^ {38}\) In experimental studies, cats treated with 6 to 10 times the recommended dose did not experience retinal toxicity.\(^ {39}\)

**Short-duration antimicrobials**

In human medicine, short-duration antimicrobial therapy, commonly, trimethoprim-sulfamethoxazole or fluoroquinolone, has become the standard treatment of acute uncomplicated bacterial cystitis in women.\(^ {40}\) The recommendations are antimicrobial-specific because not all antimicrobials have comparable efficacy when given as only a 3-day treatment. Benefits of shorter therapy include better compliance, lower cost, and decreased adverse effects.\(^ {40}\) The goal of treatment is to decrease the bacterial load enough to control clinical signs with the immune system eliminating remaining organisms.

Two recent prospective, randomized studies evaluated short-duration treatment in dogs with uncomplicated bacterial UTI. The first study compared 3-day high-dose enrofloxacin (n = 35, 20 mg/kg orally every 24 hours) to standard doses of amoxicillin-clavulanic acid (n = 33, 13.75–20 mg/kg orally every 12 hours).\(^ {41}\) Clinical and microbiological cure was evaluated 7 days after antimicrobial discontinuation and short-term, high-dose treatment was not inferior to standard treatment. The second study was double-blinded and compared 3-day trimethoprim-sulfamethoxazole (n = 20, 15 mg/kg orally every 12 hours) plus 7-day placebo to 10 days of cephalexin (n = 18, 20 mg/kg orally every 12 hours).\(^ {42}\) There was no significant difference in the short-term (4-day after treatment) and long-term (30-day after treatment) clinical and microbiological cure rates between treatment groups. Clinical cure at 30 days was 50% to 65% and microbiological cure was 20% to 44%.\(^ {42}\) Additional studies are needed to determine the appropriate treatment duration for uncomplicated bacterial UTI.

**Pyelonephritis**

Antimicrobial therapy should be initiated while waiting for the culture and sensitivity results. Empirical antimicrobials should have efficacy against gram-negative bacteria, the most common pathogens; fluoroquinolones are a good first choice (see Table 2). Acute pyelonephritis requires hospitalization for parenteral antimicrobial therapy and
intravenous fluids. Parenteral therapy should be continued until patients will eat and drink normally and azotemia is no longer improving with intensive therapy; infections should then be treated as complicated UTIs, with a minimum of 6 to 8 weeks of antibiotics and regular monitoring for recurrence of infections during and following therapy. Chronic pyelonephritis should be treated as complicated UTIs as well, but patients do not usually require hospitalization at initial diagnosis.

Prostatitis
The blood-prostate barrier is compromised with acute prostatitis and an appropriate antimicrobial should be selected based on culture and sensitivity. Treat as a complicated UTI for a minimum of 4 weeks. Antimicrobials must be selected more carefully in cases of chronic prostatitis because the blood-prostate barrier is generally intact (see Table 2). Nonionized, basic, lipid-soluble antimicrobials have the best penetration into the prostatic tissue. Drugs such as trimethoprim-sulfamethoxazole, chloramphenicol, and enrofloxacin (but not ciprofloxacin) are excellent choices. Examples of drugs with low-lipid solubility and poor diffusion across the blood-prostate barrier include penicillin and cephalothin. Antimicrobials are given for a minimum of 6 to 8 weeks. Culture of prostatic fluid should be performed before and after discontinuation of antimicrobials.

Castration is recommended as an adjunctive treatment to medical management to help reduce the prostatic size, speed recovery, and decrease recurrence. Finasteride, 5α-reductase inhibitor, may be considered in valuable breeding animals or for owners that refuse surgery.

Catheter-associated urinary tract infection
Although it seems logical to administer antimicrobial agents while an indwelling urinary catheter is inserted in an effort to decrease iatrogenic infection, the practice is strongly discouraged. Concomitant oral or parenteral administration of antimicrobial agents during indwelling urethral catheterization does not prevent development of bacterial UTI and promotes infection caused by multidrug-resistant bacteria.

Antifungals
Fluconazole is recommended as initial treatment in most patients because of the high margin of safety, sensitivity of most strains of Candida spp, and excretion of active drug into urine in high concentrations. Candida spp other than C albicans are more likely to be resistant to fluconazole, and antifungal sensitivity testing is recommended to determine if a higher dose of fluconazole is appropriate or if another drug should be used. Although amphotericin B is renally excreted and achieves high concentration in urine, it is not often used because it is parenterally administered and nephrotoxic. Other commonly used antifungal drugs, including itraconazole and ketoconazole, are not renally excreted in active form.

Secondary fungal UTI occurs because of shedding of organisms into urine in patients with systemic infections. Organisms most commonly associated with urine shedding are Aspergillus spp in dogs (particularly German shepherd dogs) and Cryptococcus spp in cats. These patients should be treated with antifungal agents standardly recommended for systemic infections.

Antivirals
Antiviral drugs have not been evaluated for animals with viral-induced urinary tract disease, and management of these patients is limited to supportive care.
NONPHARMACOLOGIC TREATMENT OPTIONS

Bacterial Interference

Bacterial interference refers to the use of low-virulence, nonpathogenic bacteria to compete with and decrease the risk of colonization and infection with more pathogenic organisms.\(^{48,49}\) Commonly used bacteria include *E. coli* (strains 83972 and HU2117) and *Lactobacillus* sp. Proposed mechanisms of action include competition for nutrients and attachment sites, bacteriocidin (antibiotic-protein) production, biofilm prevention, and host immunomodulation.\(^{48}\)

This treatment strategy is in its infancy even in human medicine, but preliminary studies are promising, especially in patients with spinal cord injury and neurogenic bladder.\(^{48–50}\) An experimental protocol for colonizing the canine urinary tract with *E. coli* 83972 has been described.\(^{51}\) Another potential future application is the prevention of catheter-associated UTI.\(^{49}\)

**Probiotics**

Alterations of vaginal microflora, in particular lactic acid–producing bacteria (LAB), may play a role in the establishment of UTI.\(^{52}\) For example, women with recurrent UTI often have depletion of vaginal *Lactobacillus* sp, whereas increased vaginal colonization with *Lactobacillus* sp is associated with reduced numbers of recurrent UTI.\(^{52}\)

In humans, *Lactobacillus* sp are the most common LAB, whereas *Enterococcus can- intestini* is the most common species in dogs.\(^{53,54}\) LAB create an acidic environment that inhibits uropathogen colonization, modulates host immune function, and may downregulate virulence factor expression of pathogenic bacteria.\(^{48}\)

Probiotics are a form of bacterial interference and recommended as a treatment and prophylaxis strategy in women. Probiotics restore *Lactobacillus* sp vaginal flora and displace potential uropathogens from the vagina.\(^{48}\) Two studies in dogs have evaluated vaginal microflora before and after probiotic administration and found no

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**Table 4**

Treatment of fungal cystitis

| For all cases | Identify and correct underlying predisposing factors | Breaches in local or systemic immunity |
|--------------|------------------------------------------------------|---------------------------------------|
| **If *C. albicans*** | Flucconazole 5–10 mg/kg PO q 12h for 4–6 wk | Urine sediment and culture at 2- to 3-wk intervals to confirm resolutionUrine sediment and culture 1 and 2 mo after therapy discontinuation |
| **If non-*C. albicans*** | Therapy based on culture and sensitivity | Monitor as aboveConsider drug penetration into urine when selecting therapy |
| **If initial treatment fails** | Repeat culture and sensitivity | Consider:Intravesicular infusion 1% clotrimazole or amphotericin BIV or SQ amphotericin BCombination fluconazole at maximum dose plus terbinafineBenign neglect, regular monitoring for disease progression |

Adapted from Pressler BM. Urinary tract infections—fungal. In: Polzin D, Bartges JW, editors. Nephrology and urology of small animals. Ames (IA): Blackwell Publishing; 2011. p. 719–21.
significant differences. However, more prospective studies are needed to evaluate the role of probiotics for lower urinary tract disease in veterinary species. Probiotics on the market vary by bacterial species, potency (number of colony-forming units), and viability. In addition, the gastrointestinal microbe has immunomodulatory effects throughout the body, and the impact of gastrointestinal probiotics on local urinary tract immune function has not been evaluated.

EVALUATION OF OUTCOME AND LONG-TERM RECOMMENDATIONS

Treatment Duration and Monitoring

**Uncomplicated bacterial urinary tract infection**

There is no consensus regarding the appropriate duration of treatment (Table 5). Uncomplicated UTIs are usually successfully treated with a standard 7- to 14-day course of an appropriate antimicrobial agent. There is some evidence that shorter treatment (ie, 3 days) is not inferior to standard durations of therapy, but more research is needed in this area. If the proper antimicrobial is chosen and administered at the appropriate dosage and frequency, clinical signs and results of a complete urine analysis should resolve within 48 hours. If possible, a urine culture should be performed 5 to 7 days after cessation of antimicrobial therapy. Uncomplicated infections are rare in cats because of their inherent resistance to bacterial UTIs, and there is typically a predisposing cause.

**Complicated bacterial urinary tract infection**

Optimal duration of therapy is unknown. Antimicrobials are usually administered for a minimum of 3 to 6 weeks. Urine should be evaluated with culture in the first week of treatment for response to therapy, before discontinuing therapy, 5 to 7 days and 1 month after therapy discontinuation.

**Catheter-associated urinary tract infection**

It is not necessary to treat bacteriuria associated with an indwelling catheter if there is no clinical or cytologic evidence of infection (Fig. 6). For patients that develop a catheter-associated UTI, treatment is more likely to be successful if the catheter can be removed. The infection may be treated as uncomplicated if there is not a history of recurrent infection and no relevant comorbidity. Otherwise, the infection should

| Table 5 | Treatment duration and monitoring |
|---------|----------------------------------|
|         | Treatment Duration | Monitoring Urine Culture |
| Uncomplicated bacterial UTI | 7–14 d | 5–7 d after discontinue antimicrobials |
| Complicated bacterial UTI | Minimum 3–6 wk | • 1 wk into therapy |
| | | • Before therapy discontinuation |
| | | • 5–7 d after discontinue antimicrobial |
| | | • 1 mo, 2 mo after treatment |
| AB | Treatment not recommended unless high risk for ascending or systemic infection |
| Fungal UTI | Minimum 6–8 wk | As above for complicated bacterial UTI |

*Data from Refs. 19,23,24*
be treated as complicated with 4 to 6 weeks of an appropriate antimicrobial based on
the culture and sensitivity. 23

Fungal urinary tract infection
Primary fungal UTIs should always be treated as complicated infections, with a mini-
umum of 6 to 8 weeks of antifungal therapy and regular monitoring during and after
cessation of therapy. 19

Prevention

Catheter-associated urinary tract infection
There are several strategies to decrease the risk of catheter-associated UTI (Box 3).

Fig. 6. Algorithm for treatment of catheter-associated UTI. (Modified from Weese JS,
Blondeau JM, Boothe D, et al. Antimicrobial use guidelines for treatment of urinary tract
disease in dogs and cats: antimicrobial guidelines working group of the international
society for companion animal infectious diseases. Vet Med Int 2011;2011:1–9.)

Box 3
Strategies to prevent catheter-associated urinary tract infection
- Avoid indiscriminate use of urinary catheters. Carefully assess the need for placing and
  retaining catheter
- Always use hand hygiene
- Use a closed collection system for indwelling catheters
- Sterile catheter placement
- Minimize duration of catheterization
- Avoid indiscriminate antimicrobial use
- Try to avoid an indwelling urinary catheter in immunocompromised patients
- Be cautious with indwelling catheter use in patients undergoing diuresis

Adapted from Siddiq DM, Darouiche RO. New strategies to prevent catheter-associated urinary
tract infections. Nat Rev Urol 2012;9:305–14; with permission.
Prophylactic antimicrobial therapy for recurrent infection  There are no good studies evaluating pulse (intermittent) or chronic low-dose prophylactic antimicrobial therapy in animals with frequent reinfections, but anecdotally, some animals may benefit (Box 3). Careful patient selection is required and the impact of promoting antimicrobial resistance should be considered. Before prophylactic treatment is undertaken, urine culture and susceptibility testing should be done to ensure that the bacterial UTI has been eradicated. For long-term prophylaxis, a drug that is excreted in high concentration in urine and unlikely to cause adverse effects is selected. Often a fluoroquinolone, cephalosporin, or a β-lactam antimicrobial is chosen. The antimicrobial agent is administered at approximately one-third of the therapeutic daily dose immediately after the patient has voided, at a time when the drug and its metabolites will be retained in the urinary tract for 6 to 8 hours (typically at night). The drug is given for a minimum of 6 months. Urine samples, preferably collected by cystocentesis (not by catheterization because this may induce bacterial UTI), are collected every 4 to 8 weeks for urinalysis and quantitative urine culture. If the sample is free of infection, then prophylactic treatment is continued. If bacterial UTI is identified, active (breakthrough) infection is treated as a complicated bacterial UTI before returning to a prophylactic strategy. If a breakthrough bacterial UTI does not occur after 6 months of prophylactic antimicrobial therapy, then treatment may be discontinued and the patient should be monitored for reinfection.

Ancillary therapies

D-Mannose  D-Mannose is used to prevent recurrent UTI, but there are no studies of clinical efficacy in veterinary patients. The D-mannose sugar competitively binds to mannose-fimbriae on certain E coli strains, thereby inhibiting adhesion to the uroepithelium. There are little data available for other bacteria that may express mannose fimbriae. An extrapolated anecdotal dose for dogs is one-quarter teaspoon per 20 pounds 3 times daily.

Methenamine  Methenamine salt is a urinary antiseptic that is converted to bacteriostatic formaldehyde in an acidic environment (urine pH <5.5). There is controversy in human medicine as to whether methenamine prevents UTI, although there is some evidence that it may be effective for short-term prophylaxis. It is unknown if the 2 salts described in the literature, hippurate and mandelate, are equally effective; the mandelate salt is difficult to find. There is limited veterinary literature on the use of methenamine in small animals, although there is a theoretic benefit. Studies of safety, efficacy, and appropriate dosing are lacking. Commonly recommended doses are 10 to 20 mg/kg orally every 12 hours (dog) and 250 mg per cat orally every 12 hours. Gastrointestinal upset and dysuria are the most commonly reported adverse events; methenamine is poorly tolerated by feline patients. Methenamine should not be used in cases of renal failure. Concurrent use of a urinary acidifier, such as DL-methionine, is usually required for maximal effect.

Cranberry  Proanthocyanidin, the “active ingredient” in cranberry, alters the genotypic or phenotypic expression of fimbriae, which subsequently inhibits E coli adherence to human bladder and vaginal epithelial cells. Studies in humans reveal inconsistent efficacy for prevention of UTI. However, in meta-analysis (n = 1049), humans supplemented with cranberry products had less UTI over a 12-month period compared with placebo.

There are few veterinary studies in healthy dogs and no feline studies. In addition, quality and potency are variable among over-the-counter products; ideally each
formulation would be tested in the species of interest. The Consensus of the Antimicrobial Guidelines Working Group of the International Society for Companion Animal Infectious Diseases is that there is insufficient evidence to support use of cranberry extract to prevent recurrent UTIs in dogs and cats.23

Local therapy Local infusions with antimicrobials, antiseptics, and dimethyl sulfoxide can be irritating and are not retained within the urinary bladder.23 Anecdotally, instillation of dilute chlorhexidine (1:100, 0.02%) and/or ethylenediaminetetraacetic acid (EDTA)-tromethamine (EDTA-Tris)62 via cystotomy tube may decrease the incidence of bacterial UTI (Bartges JW, personal communication, Knoxville, TN, 2014). In a small human study, bladder irrigation with dilute 0.02% chlorhexidine significantly decreased postoperative bacteriuria, although it did not eliminate pre-existing infection and did not appear to damage the bladder mucosa.63 It has been postulated that EDTA-Tris has synergistic effects with systemic antimicrobials64 as well as local chlorhexidine irrigation.53 Proposed mechanisms included divalent ion binding causing alteration of bacterial DNA synthesis, cell wall permeability, and ribosomal stability. In additional, in vitro studies suggest that the presence of EDTA-Tris reduces the minimum inhibitory concentration for various antimicrobial drugs.64 In a small study (n = 17 dogs, n = 4 with chronic cystitis) daily local infusion via sterile urinary catheter (25 mL EDTA at 37°C) for 7 days was well tolerated and dogs had negative urine cultures up to 180 days after treatment.64 Additional studies are needed to determine the short- and long-term effects of EDTA-Tris therapy.

TREATMENT RESISTANCE/COMPLICATIONS

Treatment Resistance

Bacterial resistance

The emergence of multidrug-resistant bacteria is concerning and has important implications for both the patient and public health. There are trends toward increasing resistance in both fecal and environmental reservoirs.65 In addition to acquiring resistance genes via plasmids, there are other bacterial strategies for persistence within the urinary tract. For example, uropathogenic *E coli* can invade and persist within the superficial bladder wall epithelial cells.65 These bacteria may remain dormant for a period of time followed by recrudescence.

Biofilms Some bacteria have the capacity for biofilm formation, which facilitates colonization.56–68 A biofilm is composed of organisms adhered together by a self-produced polysaccharide matrix.66 It has been suggested that the bacteria within the biofilm become sessile; they are protected from the immune system, are antimicrobial, and inherently are resistant to shear forces of removal.66 In humans, bacteria with the capacity to produce biofilms have been associated with AB.55,66 Biofilms are also implemented in the development of catheter-associated UTI.69

Strategies to prevent catheter-associated biofilms include using (1) materials that are less amendable to biofilm formation and (2) coatings or surface modifications that decrease biofilm formation. For example, silicone catheters are preferred over latex because scanning electron microscope imaging reveals that latex surfaces are more irregular and promote microbial adherence.49 An example of an agent used for catheter coating is the antiseptic chlorhexidine. In a veterinary prospective study (n = 26 dogs) evaluating biofilm formation on indwelling urinary catheters, sustained-release varnish of chlorhexidine-coated urinary catheters statistically decreased biofilm formation.69 There are an array of other catheter
coatings and modifications to decrease bacterial adherence and biofilm formation that have primarily been studied in a research setting, including silver coating, nanoparticles, iontophoresis, antimicrobials, urease and other enzyme inhibitors, liposomes, and bacteriophages. Other novel strategies include quorum sensing inhibitors and vibroacoustic stimulation (Box 4). A detailed discussion of comparison is beyond the scope of this article and the reader is referred elsewhere.49

Some oral antimicrobials, in particular combination therapy with clarithromycin, have shown promise in vitro for antibiofilm activity. For example, *Pseudomonas aeruginosa* biofilm was eliminated by a synergistic combination of clarithromycin and ciprofloxacin.70 Likewise, combination therapy of clarithromycin with fosfomycin was more effective than either treatment alone to reduce *Staphylococcus pseudintermedius* biofilm.71 In vivo studies are needed to further evaluate the efficacy of these therapies.

**Fungal resistance**

Infections that fail to respond completely to fluconazole should be recultured and antifungal sensitivity testing performed (see Table 4). Some susceptible isolates may

| Strategy                  | Definition                                                                 | Mechanism of Action                                       |
|---------------------------|---------------------------------------------------------------------------|------------------------------------------------------------|
| Silver coating            | Bactericidal activity of silver ion by inhibiting enzymatic pathways and disrupting the cell wall |
| Nanoparticles             | Nanometer-sized particles that attach to and penetrate bacterial cells     | Disrupt cell membranes via lipid peroxidation and interacting with DNA |
| Iontophoresis             | Application of an electrical field with low intensity direct current       | Bioelectric effect—enhance antimicrobial efficacy against bacteria within biofilms |
| Urease and other enzyme inhibitors | Eg, acetohydroxamic acid, fluorofamide, *N*-acetyl-**d**-glucosamine-1-phosphate acetyltransferase inhibitors | In vitro, reduce encrustation and alter biofilm integrity |
| Liposomes                 | Act as carriers for hydrophobic and hydrophilic drugs                      | Increase drug half-life, decrease adverse effects, protect drug from environment |
| Bacteriophages            | A virus that selectively infects bacteria                                  | Bacteriophage rapidly divides within bacteria and lyses. Bacteria can develop resistance |
| Quorum sensing inhibitors | Quorum sensing describes a system of molecular signaling (ie, autoinducers) that controls population density and gene expression. Necessary for bacteria to develop the biofilm phenotype | Eg, *Delisea pulchra* algae produces a molecule that inhibits autoinducer signaling |
| Vibroacoustic stimulation | Low acoustic waves form a vibrating coat along the catheter surface        | Inhibit bacterial adhesion and quorum-sensing electrical gradients |

Adapted from Siddiq DM, Darouiche RO. New strategies to prevent catheter-associated urinary tract infections. Nat Rev Urol 2012;9:305–14; with permission.
respond to intravesicular administration of 1% clotrimazole or amphotericin B.\textsuperscript{19,72,73} Urinary alkalinization has also been historically proposed as adjunctive therapy in patients with fungal UTI, because increased urine pH may inhibit fungal growth. However, this is not currently favored for treatment of fungal UTI in humans and is of questionable efficacy in veterinary patients.\textsuperscript{19}

**Complications**

*Magnesium ammonium phosphate (struvite) urolithiasis*

*Staphylococcus* spp and *Proteus* spp, and more rarely *Corynebacterium* spp, *Klebsiella* spp, and *Ureaplasma* spp, may produce urease (Box 5). This enzyme hydrolyzes urea to ammonia, which buffers urine hydrogen ions, forming ammonium ions, increasing urine pH, and increasing dissolved ionic phosphate. In the presence of magnesium, magnesium ammonium phosphate (struvite) may precipitate around a nidus to form uroliths (Fig. 7). Bacteria are incorporated into the urolith matrix, and thus, should be considered complicated UTIs because of poor antimicrobial penetration. Greater than 90% of struvite uroliths in dogs are induced by urease-producing bacteria, whereas struvite uroliths in cats are commonly sterile (ie, not associated with bacterial UTI). Struvite uroliths can be dissolved through a combination of dietary therapy and appropriate antimicrobial therapy; following dissolution or removal, preventing urolith recurrence requires preventing reinfection. For dogs that are uncomfortably symptomatic from urocystolithiasis and/or fail medical management, minimally invasive procedures, such as laser lithotripsy, laparoscopic-assisted cystotomy, or cystotomy, may be considered.

*Polypoid cystitis*

Chronic bacterial infections may induce microscopic or macroscopic bladder mucosal proliferation and intramural accumulation of inflammatory cells. Polypoid cystitis occurs when epithelial proliferation is severe, resulting in masslike lesions or diffuse thickening of the bladder wall (Fig. 8).\textsuperscript{74,75} Gross differentiation of polypoid cystitis from bladder wall neoplasms is not reliable; however, polypoid cystitis is more likely to develop in the bladder apex (vs transitional cell carcinomas, which are more commonly found in the bladder trigone), is more commonly botryoid in appearance rather than fimbriated, and is not as grossly vascular as transitional cell carcinomas. *Proteus* spp may be more commonly associated with development of these lesions.\textsuperscript{74,75} Polypoid cystitis lesions are niduses of deep-seated bacterial infection and should be treated as complicated UTIs. In some cases long-term antimicrobial

| Box 5 | Complications of urinary tract infection |
|-------|-----------------------------------------|
| *Potential complications of UTI* | |
| • Resistant infection | |
| • Polypoid cystitis | |
| • Emphysematous cystitis | |
| • Magnesium ammonium phosphate (struvite) urolithiasis | |
| • Pyelonephritis | |
| • Prostatitis | |
| • Prostatic abscess | |
therapy may result in successful resolution of lesions. However, partial cystectomy results in more rapid resolution of clinical signs, is likely associated with improved rates for long-term resolution of infection, and allows shorter antimicrobial treatment courses.75

**Emphysematous cystitis**

Emphysematous cystitis refers to accumulation of air within the bladder wall and lumen secondary to infection with glucose-fermenting bacteria. Most cases are due to *E coli* infection, but *Proteus* spp, *Clostridium* spp, and *Aerobacter aerogenes* have also been reported.76,77 Emphysematous cystitis most commonly develops in dogs and cats with diabetes mellitus because of the high concentration of fermentable substrate.77 Treatment of emphysematous cystitis should be as described for complicated UTI; if glucosuria is present, then appropriate treatment should be initiated for the underlying cause.

**Fig. 7.** Lateral survey abdominal radiograph of infection-induced struvite urocystourethroliths in a 3-year-old spayed female Irish setter.

**Fig. 8.** Cystoscopic image of a urinary bladder polyp with cystitis due to *E coli* in a 6-year-old spayed female Irish setter.
**Pyelonephritis**

Although no systematic reviews of pyelonephritis in dogs or cats have been performed, animals with systemically compromised immunity (ie, hyperadrenocorticism, diabetes mellitus), dogs or cats with CKD, and patients with any cause of vesicoureteral reflux are likely predisposed to development of pyelonephritis. Chronic pyelonephritis is likely underdiagnosed as a cause of renal failure in dogs and cats and should be especially considered in patients with previously stable CKD that have unexpected worsening of azotemia (ie, "acute-on-chronic" renal failure).

**Prostatic abscessation**

Prostatic abscessation is a sequela to prostatitis and is characterized by purulent fluid accumulations within the prostatic tissue. Clinical signs are variable and dependent on the size and extent of the abscess as well as systemic involvement. Prostatic abscesses are generally easily identified with ultrasonography and the goal of therapy is to provide drainage either through ultrasound-guided percutaneous drainage or surgery. Surgical options include partial prostatectomy and prostate omentalization.14

**SUMMARY**

- Determining whether an infection is uncomplicated or complicated is essential to guide the diagnostic and therapeutic plan.
- Recurrent infections are complicated infections and may be relapsing, refractory/persistent, reinfection, or superinfection.
- Antimicrobials are the cornerstone of treatment of bacterial UTI and, ideally, selected based on culture and sensitivity.
- There is limited literature to support preventative therapies; identification and resolution of underlying causes are essential.

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