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CHAPTER 89

Bacterial Infections of the Genitourinary Tract

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Overview of Bacterial Infections of the Genitourinary Tract

Causes: The most common cause of genitourinary tract infections is *Escherichia coli*, but other gram-negative bacteria, staphylococci, and streptococci may also be involved. Anaerobic bacterial infections are rare causes of genitourinary tract infections but may be involved in pyometra.

Geographic Distribution: Worldwide

Major Clinical Signs: Dysuria, hematuria, or pollakiuria may occur with lower urinary tract infection, although some infections are subclinical. Acute pyelonephritis, prostatitis, and pyometra may be accompanied by fever or abdominal pain. Lethargy, inappetence, vomiting, or diarrhea may occur if sepsis develops. Pyometra may be accompanied by abdominal distention and/or a vaginal discharge. Prostatitis may be accompanied by dysuria, dyschezia, and a purulent or hemorrhagic urethral discharge.

Differential Diagnoses: Differential diagnoses for suspected bacterial cystitis include idiopathic/interstitial cystitis (cats), bladder neoplasia, or cystolithiasis. Differentials for bacterial pyelonephritis include nephrotoxin exposure, leptospirosis, fungal pyelonephritis, or protozoal nephritis. Pregnancy, mucometra, or hydrometra are differentials for pyometra, and benign prostatic hyperplasia, paraprostatic cysts, and prostatic neoplasia are differentials for prostatitis.

Human Health Significance: Multidrug-resistant uropathogens from dogs and cats may have the potential to colonize human patients, but this requires further study.

Bacterial infections of the genitourinary tract include uncomplicated and complicated lower urinary tract infections (UTIs); prostatitis; pyelonephritis; renal abscesses; epididymitis and orchitis; and vaginitis, metritis, and pyometra. Infections of the genitourinary tract usually follow impairment of normal host defenses and invasion by bacteria that are part of the normal flora. Less commonly, infection results from hematogenous spread of bacteria to urogenital organs. Specific pathogens such as *Leptospira* spp. that injure the kidneys secondary to systemic infection are described elsewhere in this book.

In healthy dogs and cats, bacteria are not found in the upper urinary tract, urinary bladder, proximal urethra, and prostate gland. Factors that prevent bacterial colonization of the bladder include the glycosaminoglycan layer that covers bladder transitional epithelium, frequent voiding, the normal urethral microflora, antimicrobial properties of urine, an appropriate host immune response, and a functional urethral sphincter. Commensal bacteria that reside in the distal urethra, prepuce, and vagina invade opportunistically when these mechanisms are disturbed. The most common pathogen involved in all genitourinary tract infections is *Escherichia coli*, which has a particular propensity to adhere to epithelial cells of the genitourinary tract. Others include coagulase-positive and coagulase-negative staphylococci; *Enterococcus* spp.; other aerobic gram-negative bacilli such as *Klebsiella*, *Proteus*, *Enterobacter*, and *Pseudomonas aeruginosa; Corynebacterium* spp.; streptococci; and mycoplasmas. Anaerobic bacteria can also be found in the genital tracts of female dogs and can contribute to pyometra and metritis when host defenses are impaired. In addition to impaired host defenses, a variety of bacterial virulence factors influence the ability of certain bacteria to ultimately invade tissues and cause disease. Virulence factors of uropathogenic *E. coli* are described in more detail in Chapter 36.

LOWER AND UPPER URINARY TRACT INFECTIONS

Etiology and Epidemiology

Bacterial UTIs are commonly diagnosed in dogs. Although mixed bacterial infections can occur, the vast majority of UTIs involve a single bacterial species.[1] The most common uropathogen isolated is *E. coli*, which accounts for approximately 50% of all isolates, followed by *Staphylococcus*, *Proteus*, *Klebsiella*, *Enterococcus*, and *Streptococcus* species. Mycoplasmas have also been isolated from dogs with UTIs, although their clinical significance can be unclear because they are usually isolated from dogs that have other disorders of the lower urinary tract, such as underlying neoplasia or cystolithiasis. Spayed females and older dogs are at increased risk for bacterial UTIs; the mean age at diagnosis is 7 to 8 years of age.[1,2] As a result of breakdown in host defense mechanisms, systemic disorders such as acute or chronic kidney disease, hyperadrenocorticism, diabetes mellitus, and systemic neoplasia also predispose dogs to UTIs (Table 89-1).

In cats, bacterial UTIs are less common than in dogs. The prevalence of bacterial UTI in cats with lower urinary tract signs (i.e., stranguria, hematuria, pollakiuria, or dysuria; hereafter referred to as LUTS) evaluated by referral institutions has ranged from just 1% to 3%,[3-5] although the prevalence was higher (23% of cystocentesis-collected specimens) in a study from Norway.[6] Most young cats with LUTS have disorders such as feline interstitial cystitis, which are not associated with bacterial infection. When UTIs do occur in *young* adult cats, they are generally secondary to catheterization, perineal urethrostomy, or rarely, congenital anatomical defects. In older cats,

TABLE 89-1

Factors That May Predispose (or Contribute) to Development of Urinary Tract Infections in Dogs and Cats

Dogs	Cats
Recessed vulva or excess vulvar folds	Perineal urethrostomy
Diabetes mellitus	Hyperthyroidism
Hyperadrenocorticism	Diabetes mellitus
Renal failure	Renal disease
Urinary catheterization	Micturition abnormalities (urinary incontinence or urinary retention)
Ectopic ureters	Urinary catheterization
Micturition abnormalities (urinary incontinence or urinary retention)	Urolithiasis
Tube cystostomy	Urinary neoplasia (rare)
Glucocorticoid treatment and possibly treatment with other immunosuppressive drugs	Immunosuppressive drug treatment?
Urethrostomy	
Urolithiasis	
Urinary neoplasia	
Proliferative urethritis	
Polypoid cystitis	

UTIs often accompany diabetes mellitus, hyperthyroidism, and/or chronic kidney disease (CKD). The prevalence of UTIs in cats with diabetes mellitus is 11% to 13%.[7,8] At two referral institutions, positive aerobic bacterial urine cultures were found in 17% and 22% of cats with CKD and 22% and 12% of cats with hyperthyroidism.[7,9] Other factors that may predispose cats to UTI are breed (Persians or Abyssinians), female sex, older age, and lower body weight,[5,8,9] although some of these risk factors may also be associated with the comorbidities mentioned earlier. As in dogs, *E. coli* is the most common infecting species in cats. Other potential uropathogens in cats include *Streptococcus* spp., *Staphylococcus* spp., *Enterococcus* spp., *Klebsiella* spp., *Pasteurella* spp., and *Enterobacter* spp.[1,8,9] Mycoplasmas are very rarely isolated from the urine of cats.[9]

Uncommon forms of bacterial UTI in dogs and cats are *encrusting cystitis* and *emphysematous cystitis*. Encrusting cystitis is caused by the gram-positive bacterium *Corynebacterium urealyticum*. Urease production by this organism leads to precipitation of large amounts of struvite and calcium phosphate within the bladder and along the bladder and urethral mucosa, and in some cases within the ureters and renal pelvis as well.[10-12] Most animals with *C. urealyticum* infections have severe LUTS. Emphysematous cystitis is characterized by the production of gas by bacteria within the urinary bladder wall (Figure 89-1). The most common cause is *E. coli*, but *Clostridium* spp. may also be involved.[13,14] Most dogs and cats that develop *E. coli* emphysematous cystitis have glucosuria (usually secondary to diabetes mellitus), and gas production may result from fermentation of glucose to gas products by *E. coli*. In the absence of glucose, proteins such as albumin may be fermented to gas. Emphysematous cystitis caused by *Clostridium perfringens* occurs in the absence of diabetes mellitus.[13,14]

Definitions applied to infections of the urinary and genital tract are shown in Table 89-2. *Simple uncomplicated UTI* is a

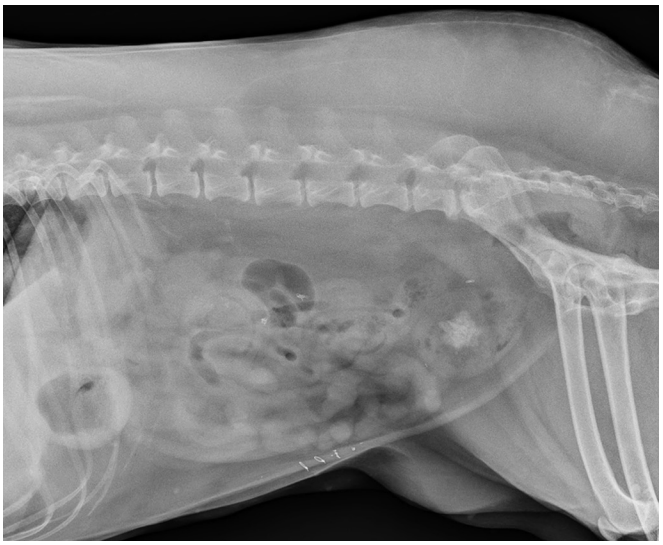

FIGURE 89-1 Lateral abdominal radiograph from a 10-year-old female spayed miniature schnauzer with emphysematous cystitis and a large, irregular cystic calculus. Irregular gas densities can see throughout the urinary bladder wall. *Escherichia coli* was cultured from a urine specimen that was obtained by cystocentesis.

TABLE 89-2

Definitions Applied to Urinary Tract Infections

Term	Definition
Simple uncomplicated UTI	Sporadic bacterial infection of the urinary bladder in an otherwise apparently healthy individual with normal urinary tract anatomy and function
Complicated UTI	UTI that occurs in the presence of an anatomic or functional abnormality or comorbidity that predisposes to persistent UTI, recurrent infection, or treatment failure
Recurrent UTI	Three or more episodes of UTI during a 12-month period
Refractory UTI	Isolation of the same microorganism more than once in the face of treatment, despite in vitro susceptibility to the antimicrobial drug used
Relapsing UTI	Isolation of the same microorganism within 6 months of apparent clearance of the infection with treatment in between positive cultures
Re-infection	Isolation of a different microorganism within 6 months of apparent resolution of a previous infection
Subclinical bacteriuria	Presence of bacteria in the urine as determined by a positive bacterial culture, in the absence of LUTS; differentiation from subclinical UTI may be difficult

sporadic bacterial infection of the bladder in an otherwise apparently healthy individual with normal urinary tract anatomy and function.[15] It has been estimated that uncomplicated UTI occurs in 14% of dogs that visit a veterinarian during their lifetime.[16] However, the actual prevalence of simple uncomplicated UTI may actually be lower, because abnormalities in host defenses probably go unrecognized in many dogs. As noted earlier, uncomplicated UTI is rare in cats. *Complicated UTIs* are associated with concurrent disorders that predispose to recurrent or persistent UTI (see Table 89-1).

Recurrence of UTI may reflect refractory (or persistent) infection, relapsing infection, or re-infection (see Table 89-2). Without the use of molecular techniques (e.g., pulsed field gel electrophoresis), it is not possible to definitively distinguish between relapse of infection and re-infection if the same bacterial species is isolated repeatedly, because different strains may be present. *Enterococcus* spp. and *Pseudomonas* spp. are isolated more commonly from dogs with persistent or recurrent UTIs than from dogs with simple uncomplicated UTIs.[2] *E. coli* can invade and form microcolonies within uroepithelial cells,[17] which may contribute to persistent infection in the face of antimicrobial treatment. Bacteria may also be able to form biofilms in association with the bladder wall ("deep seated" infections), but studies that document this in the dog are lacking.

Subclinical (or asymptomatic) bacteriuria is a term used in human medicine to describe the presence of bacteria in the urine as determined by a positive bacterial culture, in the absence of LUTS. This has generally been referred to as *subclinical UTI* in the veterinary literature. The use of the term *subclinical bacteriuria* in animals and its distinction from *infection* (which implies invasion of host tissues by bacteria and the associated inflammatory response) has been controversial, because subtle signs of infection (such as bladder pain, pollakiuria, or intermittent hematuria) may not always be detected. The term *subclinical UTI* could perhaps be applied to dogs and cats if cytologic evidence of infection (e.g., pyuria or hematuria) is present,[15] but in human patients, the term subclinical bacteriuria is used even when pyuria is present. Subclinical bacteriuria or subclinical UTIs are commonly detected in dogs and cats, especially those with underlying endocrinopathies, renal failure, or neurologic disease, as well as dogs treated with glucocorticoids or cyclosporine.[7,8,18-20] In a study of dogs treated with glucocorticoids for dermatologic disorders, 18% of 127 dogs had bacteriuria in the absence of clinical signs, whereas none of 94 dogs that had not received glucocorticoids had bacteriuria.

Pyelonephritis most often occurs when bacteria ascend into the renal pelvis and parenchyma from the lower urinary tract. Less commonly, hematogenous spread to the kidney occurs. A single bacterial species (most often *E. coli*) is isolated from the urine of approximately three quarters of dogs with pyelonephritis; two species are isolated in fewer than 10% of dogs and three species from fewer than 5% of dogs. Pyelonephritis may be acute or chronic. Strains of *E. coli* that cause pyelonephritis have greater ability to adhere to cells than strains that cause cystitis. Adhesins located on the tip of *E. coli* fimbriae (P fimbriae) adhere to glycolipid residues on tubular, collecting duct, and bladder epithelial cells. In human pyelonephritis, both P and type I fimbriae are important in colonization of the renal pelvis.[21,22] Other *E. coli* virulence factors associated with pyelonephritis include hemolysin, cytotoxic necrotizing factor, the iron scavenger aerobactin, and a serum protease known as Sat. Fimbriae are also important in the pathogenesis of *Proteus* pyelonephritis.[23] The renal medulla is more sensitive to colonization than the cortex, possibly owing to impaired host defenses in a high osmolality, low pH, and low blood flow milieu. Organisms adhere to pelvic, distal, and proximal tubular epithelium and have been observed intracellularly. Considerable renal injury results from the inflammatory response to infection. Aggregation of neutrophils within capillaries and induction of vascular spasm by bacterial toxins and/or cytokines can contribute to renal ischemia.

Clinical Features

Clinical Signs

Clinical signs of lower UTI may be absent, or include signs such as dysuria, hematuria, stranguria, and pollakiuria. Cats may urinate outside the litter box (periuria or inappropriate urination). Rarely, animals with lower UTIs may be lethargic, but fever and inappetence are not present. Acute or acute-on-chronic pyelonephritis may result in inappetence, lethargy, variable fever, hematuria, and clinical signs of uremia, such as vomiting and diarrhea. Polyuria and polydipsia may also be present, or dogs with severe disease may be anuric. Dogs and cats with chronic pyelonephritis may show no signs, or only polyuria and polydipsia.

Physical Examination Findings

Physical examination findings in dogs or cats with lower UTIs may be unremarkable, or urine or urine scalding may be identified around the perineum. A strong ammonia-like odor may be present. Sometimes, pain can be detected on palpation of the urinary bladder of dogs or cats with bacterial cystitis, and abdominal or flank pain may be noted in animals with acute pyelonephritis. The urinary bladder is often small as a result of pollakiuria. A thickened bladder wall may also be palpated. If a large, turgid bladder is present in dogs or cats with a UTI, urethral obstruction due to neoplasia, calculi, proliferative urethritis, or encrusting cystitis should be suspected. Underlying disorders that predispose to lower UTIs may also be apparent (such as vulvar fold dermatitis).

Dogs and cats with severe pyelonephritis may show signs of lethargy, dehydration, variable fever, and evidence of severe sepsis or septic shock (e.g., tachycardia or bradycardia, tachypnea, or prolonged capillary refill time).

Diagnosis

Diagnosis of UTIs is based on the clinical signs present, laboratory abnormalities, imaging findings, and culture of urine. The presence of fever or leukocytosis in addition to a positive bacterial urine culture should increase suspicion for concurrent bacterial pyelonephritis, prostatitis, or pyometra (see relevant sections later in this chapter). Ultrasound examination findings also can support the diagnosis and assist in the identification of underlying disorders such as neoplasia, anatomic abnormalities, or the presence of calculi or foreign material. At a minimum, collection of urine by cystocentesis followed by complete urinalysis (with sediment examination) and quantitative aerobic bacterial urine culture are recommended to properly confirm the presence of bacterial UTI for dogs or cats with signs of lower urinary tract disease.[15] Additional diagnostics

are indicated for animals that have recurrent LUTS or those with systemic signs such as fever, weight loss, or inappetence. The owners of animals diagnosed with what appears to be uncomplicated UTI should be advised that other underlying disease may be present.

Laboratory Abnormalities

Complete Blood Count and Serum Biochemical Tests

Animals with infections confined to the lower urinary tract typically have no hematologic or serum biochemistry abnormalities. Animals with pyelonephritis may have mild anemia, leukocytosis due to a neutrophilia, bandemia, and monocytosis. A degenerative left shift, toxic neutrophils, and thrombocytopenia may also be present. The serum biochemistry panel may show azotemia and sometimes hypoalbuminemia and/or electrolyte abnormalities.

Urinalysis

Findings on the urinalysis in dogs and cats with UTIs include isosthenuria, pyuria, hematuria, proteinuria, and/or bacteriuria. Animals with pyelonephritis may have cylindruria, and small amounts of glucose may be present as a result of altered proximal tubular function. However, the urinalysis can also be normal, even in dogs and cats with pyelonephritis. Infections with urease-producing bacteria such as staphylococci, *Proteus* spp., and *C. urealyticum* can be associated with a high urine pH and struvite crystalluria.

Coagulation Profile

Evidence of coagulation abnormalities may be present in animals with severe pyelonephritis that develop severe sepsis or septic shock (see Chapter 86).

Diagnostic Imaging

Plain Radiography

Dogs or cats with bacterial cystitis generally have no radiographic abnormalities. The urinary bladder may be small if pollakiuria is present. Emphysematous cystitis is characterized by the presence of radiolucencies within the bladder lumen and/or in association with the bladder wall (see Figure 89-1). Radiopaque cystic or renal ("staghorn") calculi may be visible in dogs with struvite calculi secondary to *Staphylococcus* spp. or *Proteus* spp. infections (Figure 89-2).

Renomegaly may be present with acute pyelonephritis, which is typically mild. The kidneys may be small and irregular in dogs or cats with chronic pyelonephritis.

Contrast Radiography

Contrast cystourethrography can be useful for diagnosis of conditions that predispose to recurrent or persistent UTIs, such as anatomic abnormalities, diverticuli, bladder or urethral neoplasia, proliferative urethritis, polypoid cystitis, or nonradiopaque calculi. Intravenous contrast urography has been used to identify pyelectasia and assist in the diagnosis of pyelonephritis, but has largely been replaced by abdominal ultrasound for this purpose, which is less invasive.

Sonographic Findings

Ultrasound examination of the urogenital tract provides information about the extent and severity of disease and underlying causes such as neoplasia, calculi, or foreign bodies. *It does not permit visualization of the entire urethra*, and so urethral abnormalities may be overlooked in some animals if only ultrasound is used to image the lower urinary tract. Ultrasound examination of the urinary bladder may be unremarkable or show a mild to moderately thickened bladder wall in dogs or cats with bacterial cystitis. Echogenicity of the urine may be present. Rarely, the bladder wall is severely thickened (Figure 89-3). Animals with emphysematous cystitis may have a hyperechoic urinary bladder wall with acoustic shadow artifacts. Shadow artifacts also occur when cystic calculi are present.

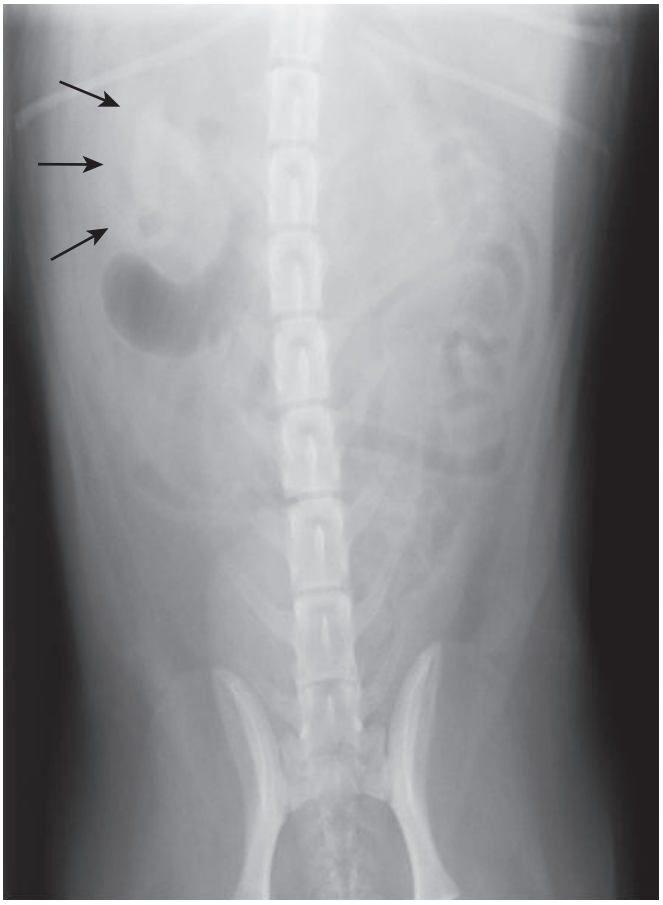

FIGURE 89-2 Dorsoventral radiograph of a 6-year-old female spayed shih tzu mix with a urinary tract infection caused by *Proteus mirabilis* and *Enterococcus faecalis* and nephrolithiasis. An opacity ("staghorn" calculus) occupies the right renal pelvis (*arrows*).

Dogs or cats with pyelonephritis may have a normal abdominal ultrasound examination; or blunting of the renal papilla, pyelectasia, irregularity of the renal contour, and/or hydronephrosis may be seen (Figure 89-4). However, pyelectasia can occur in animals with normal renal function, diuresis, and outflow tract obstruction, and there is considerable overlap in the extent of dilatation between groups.[24] The renal pelvis of dogs and cats with severe pyelonephritis may contain hyperechoic debris.[25] Sometimes the surrounding mesentery is hyperechoic, and perinephric anechoic fluid is present as a result of localized peritonitis. Other nonspecific findings in pyelonephritis include increased renal cortical echogenicity and decreased corticomedullary definition.

Cystoscopy

Cystoscopy can be a useful diagnostic procedure to identify underlying causes of recurrent UTIs in dogs and cats, after

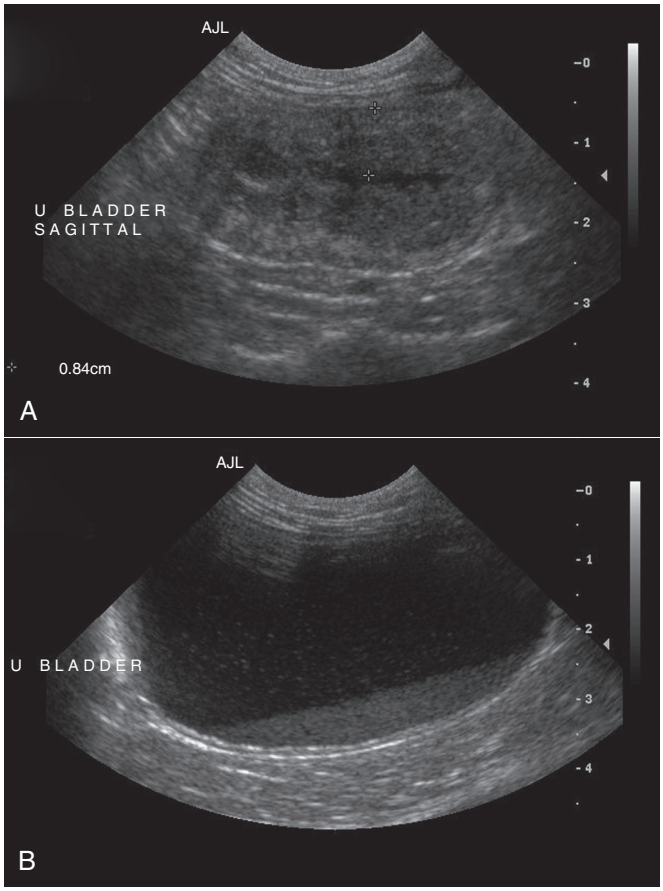

FIGURE 89-3 Ultrasound images of the bladder of an 18-year-old female spayed domestic shorthair cat with diabetes mellitus, generalized osteoarthritis, a cervical myelopathy, and L4-L6 disc space compression and recurrent urinary tract infections. The cat had severe lower urinary tract signs (hematuria, pollakiuria, and stranguria), and a hemolytic *Escherichia coli* was isolated from the urine. **A,** The wall of the urinary bladder is markedly thickened. **B,** Resolution of bladder wall thickening after treatment with marbofloxacin for 3 weeks, which also resolved the clinical signs.

evaluation has been performed first to evaluate for metabolic abnormalities such as renal failure, hyperadrenocorticism, or diabetes mellitus. Cystoscopy or contrast computed tomography are the most sensitive diagnostic tests for identification of ectopic ureters. Cystoscopy can also be used to obtain mucosal uroepithelial biopsies for histopathology and culture.

Microbiologic Tests

Isolation and Identification

Quantitative aerobic bacterial culture and susceptibility is always indicated for dogs or cats with UTIs before starting antimicrobial drugs, because of the possibility of antimicrobial drug resistance, which is well recognized among *E. coli* strains isolated from dogs and cats with UTIs.[26,27] Guidelines for diagnosis of bacterial UTIs in dogs and cats have been published.[15] Ideally, urine should be collected by cystocentesis; if this is not possible, urethral catheterization can be used. Although any pathogens isolated from specimens collected by cystocentesis are likely significant, bacterial contamination from the skin is possible; therefore, the presence of more than 10^3 CFU/mL of bacteria is considered clinically significant. If specimens are collected via catheterization, colony counts that exceed 10^4 CFU/mL for male dogs and 10^5 CFU/mL for female dogs are considered clinically significant.[15] Free-catch (midstream voiding) specimen collection should not be used for

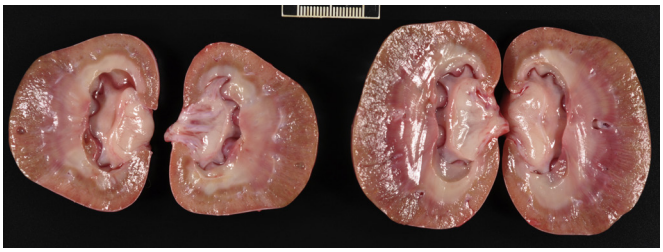

FIGURE 89-4 Kidneys of a 2-year-old male neutered German shepherd with diabetes mellitus and chronic pyelonephritis secondary to *Klebsiella pneumoniae* infection. The kidneys are bilaterally asymmetrical; the right kidney is larger than the left. There are several small, cortical subcapsular cysts, and the kidneys have an irregular conformation with markedly shrunken poles and are fibrotic. The renal parenchyma at the poles is markedly collapsed from the capsule to the pelvis, and the pelvis is uniformly dilated. (Image courtesy University of California, Davis, Veterinary Anatomic Pathology Service.)

dogs or cats because it is highly susceptible to contamination. A positive aerobic bacterial culture of a cystocentesis-collected urine specimen confirms the presence of bacterial infection in animals that have LUTS. Culture can also help to differentiate re-infection from relapse should a UTI return; if the second isolate is a different bacterial species or has a different antibiotic susceptibility pattern (also known as an *antibiogram*), reinfection is likely.[15] Specimens for culture should be refrigerated immediately and submitted to the laboratory as soon as possible. For specimens that reach the laboratory more than 24 hours after collection, culture results should be interpreted with caution, because false-negative and false-positive test results can occur. For dogs and cats with recurrent UTIs that undergo surgery, culture of a bladder wall biopsy or of cystoliths should be considered.

Inexpensive urine "paddles" are available for in-house veterinary diagnosis of UTIs. One type consists of two different types of agar on either side of a plastic paddle (see also Chapter 3, Figure 3-6). The media are inoculated with urine collected by cystocentesis, and the paddles are then incubated and examined daily for growth. These paddles can be useful screening tools when client finances do not permit submission of specimens to a microbiology laboratory for culture, and they allow identification of significant bacterial growth by comparison of colony numbers to a chart provided by the manufacturer. They also reduce the effect of delays in submission of specimens to a laboratory. However, they may be inaccurate for identification of bacterial species involved, especially when mixed infections are present.[28] Paddles may not yield reliable results if submitted to a laboratory for confirmation and minimum inhibitory concentration (MIC) testing. If used, and growth is detected on the paddle within 24 hours, saved (refrigerated) urine or a freshly collected urine specimen should be submitted to a microbiology laboratory for culture and susceptibility testing. Another type of in-house culture system provides limited information on bacterial antibiotic susceptibility (Flexicut Vet, Atlantic Diagnostics), but requires further study. In-house bacterial cultures should only be performed in clinics with appropriate laboratory facilities, proper biosafety level containment and waste management, and adequately trained personnel.[15] Accurate susceptibility testing is difficult to perform and interpret, and whenever possible, submission to a veterinary diagnostic laboratory that adheres to Clinical and Laboratory Standards Institute (CLSI) guidelines is recommended.

For animals with indwelling urinary catheters, some bacteriuria is expected due to compromise of host immune defenses. Culture is indicated if clinical signs of infection are present

(e.g., gross hematuria, pyuria, or suspected bacteremia).[15] Optimally, the catheter should be removed and cystocentesis performed after the bladder is allowed to fill with urine. Alternatively, the catheter could be removed, replaced with a new catheter, and a urine specimen collected through the catheter after several milliliters of urine are removed to clear the catheter. Urine culture should never be submitted from specimens collected from the urine bag, and there is no indication to culture the catheter tip.

When pyelonephritis is present, bacteria cultured from the urine are usually those present in the upper tract. A negative urine culture does not rule out bacterial pyelonephritis. In some cases, cytology and culture of ultrasound-guided aspirates of the renal pelvis (pyelocentesis) may assist in the diagnosis of pyelonephritis. Blood cultures could also be considered in animals with acute pyelonephritis, especially when signs of sepsis are present.

Laboratories that perform and report susceptibility testing for uropathogens should adhere to local regulatory guidelines (such as the CLSI). Breakpoints for systemic infections also apply to UTIs (see Chapter 3 for a discussion of breakpoints). However, many antimicrobials achieve much higher concentrations in the urine than they do in the serum. Therefore, if routine serum susceptibility testing is performed for a dog or cat with a lower UTI and normal renal function, some antimicrobials may eradicate the UTI, despite in vitro resistance. This is especially true for treatment of staphylococcal UTIs with penicillins and cephalosporines. Urinary breakpoints are available for ampicillin or amoxicillin in dogs (≤8 µg/mL), amoxicillin-clavulanate in dogs and cats (<8/4 µg/mL), and nitrofurantoin. Urinary breakpoints (reported as urine MICs by the laboratory) should be used only when infection is confined to the lower urinary tract.

Pathologic Findings

Pathologic findings in dogs with bacterial cystitis and pyelonephritis depend on the chronicity of the infection, the underlying cause, and the uropathogens present. Acute infections are associated with a dense neutrophilic infiltrate in tissues on histopathology and intralesional bacteria may be identified. Chronic infections may be associated with histiocytic or lymphoplasmacytic infiltrates.

Treatment and Prognosis

Treatment of UTIs consists of removal or management of the underlying cause(s) of infection, followed by antimicrobial drug treatment. Antimicrobial drug treatment alone without attention to an underlying cause frequently leads to recurrent infection and selection for resistant bacteria. Because of the increasing prevalence of multidrug-resistant (MDR) *E. coli* and staphylococci in dogs and cats with UTIs, consideration should be given to delaying antimicrobial drug treatment until the results of culture and susceptibility are available, provided the patient is stable and sepsis is absent. This is especially true for dogs and cats with recurrent UTIs that have a history of antimicrobial drug treatment. Empiric treatment while awaiting the results of culture and susceptibility could be considered to relieve discomfort, if present; however, some dogs respond well to analgesic therapy (e.g., tramadol) pending susceptibility test results. When sepsis is present, initial treatment should be broad-spectrum and cover MDR gram-negative bacteria (see Chapter 86).

Uncomplicated UTIs

In most situations, rational choices for initial treatment of uncomplicated UTIs include amoxicillin or trimethoprim-sulfonamide (TMS) (Table 89-3), although TMS has the potential to cause significant adverse effects in dogs. Amoxicillin–clavulanic acid could be considered if practice/regional susceptibility trends suggest a high (>10%) prevalence of β-lactamase production by uropathogens isolated (i.e., >10% of bacteria isolated in a practice show susceptibility to amoxicillin–clavulanic acid but not amoxicillin).[15] However, amoxicillin–clavulanic acid may need to be given q8h to ensure significant concentrations of clavulanic acid in the urine. Once culture and susceptibility results are available, the chosen antimicrobial drug should either be continued (if a clinical response has occurred) or switched to an alternative drug with activity against the pathogen that enters urine in high concentrations. A treatment duration of 7 days has been suggested.[15] One study showed that treatment of dogs that had uncomplicated UTIs with high-dose enrofloxacin (20 mg/kg) for 3 days was not inferior to treatment with amoxicillin–clavulanic acid for 14 days.[29] Additional studies of dogs with naturally occurring UTI that evaluate short durations of treatment with other antimicrobial drugs such as amoxicillin or TMS are needed. Studies are also needed to evaluate the need for posttreatment cultures to determine whether resolution of infection has occurred.[15]

Complicated UTIs

Investigation to identify an underlying cause is strongly recommended for animals with complicated UTIs. Referral should be considered for advanced imaging and diagnostic tests to evaluate the patient for predisposing factors. The choice of antimicrobial drug should be based on culture and susceptibility test

TABLE 89-3

Suggested Initial Treatment for Stable Dogs or Cats with Genitourinary Tract Infections Pending Culture and Susceptibility Results

Disease	Drug	Dose (mg/kg)	Route	Interval (hours)
Bacterial cystitis or pyometra	Amoxicillin *or*	11-15	PO	8
	Trimethoprim-sulfadiazine *or*	15*	PO	12
	Amoxicillin–clavulanic acid	12.5-25	PO	8
Pyelonephritis, prostatitis	Enrofloxacin *or*	10-20 (dogs)	PO	24
	Marbofloxacin *or*	2.7-5.5	PO	24
	Orbifloxacin	7.5	PO	24

See Table 86-8 for options for severe sepsis.
*Based on trimethoprim plus sulfadiazine concentration.

results, and preference should be given to drugs that are excreted in the urine in active form. If excreted in the urine, drugs with intermediate susceptibility could be used to treat UTIs that are resistant to other appropriate drug choices; however, a higher dose (for concentration-dependent antimicrobials) or dosing frequency (for time-dependent antimicrobials) should be considered in these circumstances. Use of nitrofurantoin could be considered for lower UTIs that are resistant to other oral antimicrobial drugs that are excreted in the urine. When mixed infections are present, ideally antimicrobial drug treatment should be directed at all organisms present. In mixed infections that involve *Enterococcus* spp., anecdotal evidence suggests that the *Enterococcus* spp. infection will resolve when the other organisms are successfully treated.[15] Typically, 4 weeks of treatment is recommended for complicated UTIs, but shorter courses may be effective. Urine culture could be considered 5 to 7 days after initiating treatment to ensure the infection is not persistent and is recommended 7 days after treatment has been discontinued. If follow-up cultures are positive, further investigation to identify an underlying cause may be required. If no clinical signs are present, management should be as for subclinical bacteriuria (see later discussion).

There is no evidence that direct instillation of antimicrobials, antiseptics, glycosaminoglycans, or dimethyl sulfoxide (DMSO) directly into the bladder via a urinary catheter is effective for treatment of recurrent UTIs in dogs. These compounds are rapidly eliminated from the bladder when the animal urinates and may be locally irritating, which may predispose further to infection with drug-resistant bacteria. Approaches used in an attempt to prevent recurrence are detailed in the Prevention section.

Subclinical Bacteriuria

Treatment may not be required for dogs or cats that lack LUTS, but could be considered for dogs or cats that have underlying immunosuppressive disorders or are receiving glucocorticoids or chemotherapeutics (which may predispose them to ascending or systemic infection). However, some animals with disorders that predispose to bacterial colonization of the bladder are continuously bacteriuric, and treatment with antimicrobial drugs only selects for colonization by resistant organisms. More evidence that supports the need for diagnosis and treatment of subclinical bacteriuria when accompanied by specific disorders such as hyperadrenocorticism, diabetes mellitus, or chronic glucocorticoid treatment is required. Bacterial virulence factors may determine whether systemic invasion occurs.[30] MDR organisms are often of low virulence and may be replaced by susceptible bacteria when antimicrobial drug pressure is removed. After that, treatment may be possible if clinical signs develop or if there is concern for ascending infection. In human patients, treatment of asymptomatic bacteriuria associated with *Enterococcus* spp. infection is not recommended.[31] Whether this is also an appropriate recommendation in dogs and cats is unclear.

Pyelonephritis

Treatment of dogs with acute pyelonephritis should be initiated immediately, without waiting for culture and susceptibility test results. Cytologic examination of stained urine sediment may assist in initial selection of an antimicrobial drug (i.e., based on the presence of rods versus cocci). The use of a fluoroquinolone that is excreted in the urine in active form (i.e., not difloxacin) is recommended for gram-negative bacterial pyelonephritis, provided regional susceptibility data do not show widespread resistance to fluoroquinolones.[15] The dosage used may need to be reduced if severe renal impairment is present. If combination treatment is initiated and antimicrobial susceptibility test results show susceptibility to only one drug, the other drug should be discontinued. Treatment for 4 to 6 weeks is recommended, although shorter periods of treatment may be effective and require further study. Dogs with acute pyelonephritis may need hospitalization and treatment with intravenous fluids and other medications for acute renal failure or sepsis. Urinalysis and culture should ideally be performed after 7 days of treatment and again 7 days after treatment has been discontinued, to ensure that infection has been eliminated. If the same organism is isolated again, then an additional antimicrobial drug with in vitro activity against the organism could be added. Struvite nephrolithiasis (such as "staghorn" calculi) or struvite cystoliths may dissolve with antimicrobial treatment, although dietary intervention may also be needed in some cases. When stones are present, antimicrobial treatment should be continued until there is no radiographic or ultrasonographic evidence of calculi and the urine is sterile. Other calculi such as calcium oxalate, urate and cystine can predispose animals to recurrent bacterial infections and, if possible, should be removed. While dissolution protocols are described for urate and cystine, they often are not as rewarding as struvite. Calcium oxalate stones are not amenable to dissolution with dietary or antimicrobial therapy.

Prevention

Prevention of lower UTIs involves identification and reversal of underlying causes of infection, such as vulvar fold dermatitis or congenital abnormalities such as ectopic ureter. Urinary catheterization should be used only when necessary and should be performed in a manner that maintains sterility as much as possible. Intermittent catheterization is preferred to placement of an indwelling catheter. If indwelling catheterization is required, a closed sterile collection system should always be used, and the catheter should be removed as soon as it is no longer required, because the risk of ascending infection increases with every day the catheter is left in place. Treatment of catheterized animals with antimicrobial drugs may increase the risk for infection[32] and so should be done only when necessary; antimicrobial drugs should not be used in an attempt to prevent urinary catheter infection. Routine antimicrobial treatment after catheter removal is not indicated unless clinical signs of UTI develop, because colonization that follows catheterization is cleared once the catheter is removed and host defenses are restored.

Many treatments for prevention of UTIs in dogs and cats with a history of recurrent disease have been considered. Currently there is no evidence that urinary antiseptics (such as methenamine) or nutritional supplements (such as cranberry juice extract) are effective in dogs or cats. Some studies of the use of cranberry extract in human patients have shown no effect.[33,34] Evidence that intermittent (pulse) therapy or chronic, low-dose antimicrobial treatment prevent recurrent UTIs is anecdotal; because it may select for resistant organisms, it is not generally recommended.

Public Health Aspects

Dogs and cats with UTIs have a potential to act as a source of MDR bacteria for humans. Similarities between uropathogenic *E. coli* isolates from dogs and those from humans have been identified,[35,36] but differences also exist.[37] Owners of pets with MDR UTIs should always wash their hands after handling their pets

and wear gloves when medications are administered, and pets should be taken to urinate away from other people and animals.

ORCHITIS, EPIDIDYMITIS, AND PROSTATITIS

Etiology and Epidemiology

Orchitis and epididymitis may occur in association with bacterial UTIs or penetrating foreign bodies (e.g., plant awns) in intact male dogs, but this is rare. Infection with *Brucella canis* should always be suspected in dogs with epididymitis (see Chapter 53).

E. coli accounts for most cases of bacterial prostatitis in dogs. Occasionally other gram-negative or gram-positive bacteria, including atypical organisms such as *Mycoplasma* spp. and *Brucella* spp., cause prostatitis. Bacterial prostatitis is extremely rare in cats.[38]

Clinical Features

Signs and Their Pathogenesis

Bacterial prostatitis in dogs may be acute or chronic. It can occur secondary to benign prostatic hyperplasia or prostatic neoplasia, most likely as a result of ascending infection secondary to altered urinary defense mechanisms. Bacterial prostatitis should be suspected in any intact male dog that develops a UTI. Dogs with bacterial prostatitis may show infertility, fever, lethargy, inappetence, weight loss, LUTS, purulent or hemorrhagic urethral discharge, abdominal pain, and sometimes a stiff gait. Tenesmus, vomiting, and diarrhea also occur in some dogs. Acute bacterial prostatitis can be accompanied by severe sepsis or septic shock (see Chapter 86). Formation of prostatic abscesses may be followed by abscess rupture and peritonitis. Dogs with chronic prostatitis may be lethargic or have no clinical signs of illness.

Physical Examination Findings

Dogs with acute bacterial prostatitis may exhibit pain on palpation of the prostate during physical examination. The prostate may be normal in size and shape, or enlarged or irregularly shaped. Fluctuant regions may be palpated if abscesses are present. Palpation should always be performed cautiously when acute bacterial prostatitis is suspected to avoid rupture of prostatic abscesses. Hemorrhagic or purulent discharge may be seen at the urethral orifice. Dogs with severe acute prostatitis may be dehydrated, febrile, obtunded, and show other signs of severe sepsis or septic shock (e.g., tachycardia or bradycardia, tachypnea, prolonged capillary refill time). Intact male dogs with bacterial orchitis or epididymitis may have testicular enlargement, hyperemia, and pain on palpation of the testicles. These findings may be present in association with prostatitis.

Diagnosis

Diagnosis of bacterial prostatitis is based on clinical signs, laboratory abnormalities, imaging findings, and culture of urine or prostatic secretions.

Laboratory Abnormalities

Dogs with acute prostatitis may have mild anemia and leukocytosis due to a neutrophilia, bandemia, and monocytosis. A degenerative left shift, toxic neutrophils, and thrombocytopenia may be present in severely affected dogs. Hypoalbuminemia and electrolyte abnormalities may be present, or there be evidence of organ dysfunction in dogs with septic shock. Hyperglobulinemia can be present in dogs with chronic prostatitis. The urinalysis may reveal abnormalities consistent with UTI.

Diagnostic Imaging

Plain and Contrast Radiography

Plain radiography is of limited value for diagnosis of bacterial prostatitis. Dogs with prostatic abscesses may have prostatomegaly (a prostate diameter >70% of the distance between the pubis and the sacral promontory), with ventral and cranial displacement of the urinary bladder.[39] Prostatic mineralization rarely accompanies chronic bacterial prostatitis in intact dogs, but when present in a neutered dog, mineralization strongly supports the presence of prostatic neoplasia.[40] Extravasation of contrast material into the prostate during retrograde contrast cystourethrography supports a diagnosis of prostatitis or prostatic neoplasia.

Sonographic Findings

Sonographic abnormalities in dogs with prostatitis include prostatic irregularity, mixed echogenicity, and focal accumulations of anechoic or hypoechoic fluid, with distance enhancement (prostatic cysts or abscessation) (Figure 89-5).[41]

Microbiologic Tests

Isolation and Identification

Many dogs with prostatitis shed bacteria into the urine, and therefore bacteria cultured from the urine are usually those involved in prostatitis. However, a negative urine culture does not rule out bacterial prostatitis, and occasionally the organisms isolated from the urine differ from those isolated from the prostate.

Collection of prostatic fluid via ejaculation, prostatic wash, or aspiration of the prostate or prostatic cysts may also be helpful

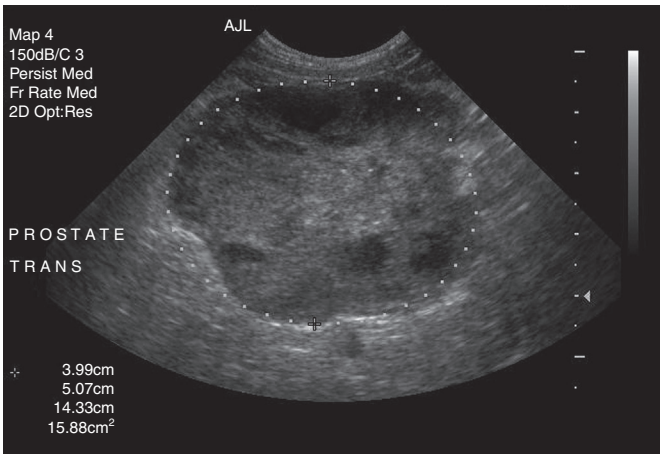

FIGURE 89-5 Ultrasound image of the prostate of a 12-year-old intact male beagle dog that had acute prostatitis due to *Escherichia coli* and associated bacterial peritonitis. The dog was seen for acute onset of anorexia and vomiting. Bloodwork revealed 2254 neutrophils/μL, 1160 band neutrophils/μL, mild hypoalbuminemia (2.4 g/dL; reference range, 2.9-4.2 g/dL), increased serum ALP activity (1338 U/L; reference range, 15-127 U/L) and increased serum total bilirubin concentration (0.5 mg/dL, reference range, 0-0.4 mg/dL). The prostate was significantly increased in size on sonographic examination and contained multiple hypoechoic nodules. There was a small quantity of ascites, which were localized in the caudal abdomen in the region of the prostate. Hemolytic *E. coli* was isolated from urine and from a prostatic aspirate. The owners elected euthanasia. Acute prostatitis and peritonitis were confirmed at necropsy.

for the diagnosis of bacterial prostatitis. Aspirates of the prostate for culture and cytology (if clinically indicated) can be done in dogs with acute and chronic prostatitis; however, dogs with acute prostatitis may require sedation for patient comfort. The presence of large numbers of bacteria (>10^5 CFU/mL) together with an inflammatory response suggests infection. Cytologic examination and culture of ultrasound-guided aspirates of prostatic abscesses has been used to assist diagnosis, but there is a risk of localized peritonitis when abscessed tissues are aspirated.

Pathologic Findings

Dogs with acute prostatitis may have infiltrates of neutrophils with or without intralesional bacteria in the prostate on histopathology. Chronic infections may be associated with histiocytic or lymphoplasmacytic infiltrates. In some cases, prostatic hyperplasia or abscess formation are identified.

Treatment and Prognosis

Acute prostatitis should be treated with an appropriate antimicrobial drug for 4 weeks. If the dog is septic, parenteral antimicrobial administration may initially be required. If inflammation is severe, any drug appropriate for treatment of UTIs may still penetrate the prostate in the acute phase.

Drug penetration is impaired in dogs with chronic prostatitis because of the blood–prostatic fluid barrier. Drugs that effectively cross the prostatic barrier of dogs include enrofloxacin, ofloxacin, marbofloxacin, trimethoprim, and chloramphenicol. Because trimethoprim-sulfamethoxazole and chloramphenicol are more likely to be associated with adverse effects when administered for prolonged periods, a fluoroquinolone such as enrofloxacin is the drug of choice for initial treatment of gram-negative bacterial prostatitis. If the MIC of the organism is between 0.5 and 1.0 µg/mL, the highest dose of enrofloxacin is recommended (20 mg/kg q24h). Clindamycin may be a reasonable choice for dogs with gram-positive bacterial prostatitis, although this is uncommon. Treatment of dogs with chronic prostatitis should continue for at least 6 weeks. Organisms may persist within the prostate of dogs with chronic prostatitis despite appropriate antimicrobial drug treatment. Cure may not be possible without castration.

Surgical castration is recommended for dogs with prostatitis and should be performed as soon as the dog is stable to undergo anesthesia and surgery. The efficacy of drugs that cause prostatic involution, such as finasteride, is not clear, but finasteride enhanced resolution of infection in a rat model of chronic prostatitis when administered with a fluoroquinolone.[42] Prostatic abscesses also must be treated surgically, although ultrasound-guided drainage together with antimicrobial drug treatment can be effective for small (e.g., <2.5 cm) abscesses. Castration and antimicrobial drug treatment alone do not effectively resolve prostatic abscesses; surgical drainage is required. Long-term, once-daily treatment with antimicrobial drugs that enter the prostate has been suggested for dogs that fail to respond to medical and surgical treatment of chronic prostatitis, as used to treat humans.[43]

Follow-up should consist of a recheck 7 to 10 days after initiating treatment. Aerobic bacterial urine culture should be considered at this time if a positive urine culture was initially present. A recheck should also be performed 1 week after discontinuation of treatment, at which time physical examination, urinalysis, urine culture, and prostatic fluid cytology and culture should be performed. Where available, prostatic ultrasound may also provide useful information at these follow-up times and, if possible, should be performed 1 week after discontinuation of antimicrobial drugs.

Prevention

Routine castration reduces the risk of prostatitis, but prostatitis can still occur in neutered animals.

VAGINITIS, METRITIS, AND PYOMETRA

Etiology and Epidemiology

Bacterial vaginitis in adult bitches is usually secondary to an underlying disorder such as neoplasia, foreign bodies (e.g., grass awn), UTI, or anatomic abnormalities such as strictures. Puppy vaginitis is thought to be a consequence of immaturity rather than bacterial infection.

Metritis results from ascending infection of the uterus. It usually occurs shortly after parturition (e.g., within a week) or after obstetrical procedures. It may be associated with clinical signs of lethargy, fever, decreased appetite, and purulent vaginal discharge.

Pyometra is an accumulation of pus within the uterus (Figure 89-6). The pathogenesis of pyometra is incompletely understood. However, in contrast to metritis, pyometra most often seems to occur as a result of increased serum progesterone concentrations, which cause cystic endometrial hyperplasia (CEH), impaired immune function, and decreased uterine contractility. The end result for some dogs and cats is opportunistic bacterial invasion, most often by *E. coli* strains that have virulence factors typical of uropathogenic isolates.[35,44] Other bacterial species that cause pyometra are similar to those that cause UTIs, with the exception that anaerobes are more often involved in pyometra, usually in mixed infections with other bacteria. CEH is not an absolute requirement for development of pyometra, and some animals with CEH never develop pyometra. Exogenous administration of estrogen (used to treat mismating) or progesterone has also been associated with pyometra.[45] Rarely, pyometra occurs in conjunction with uterine

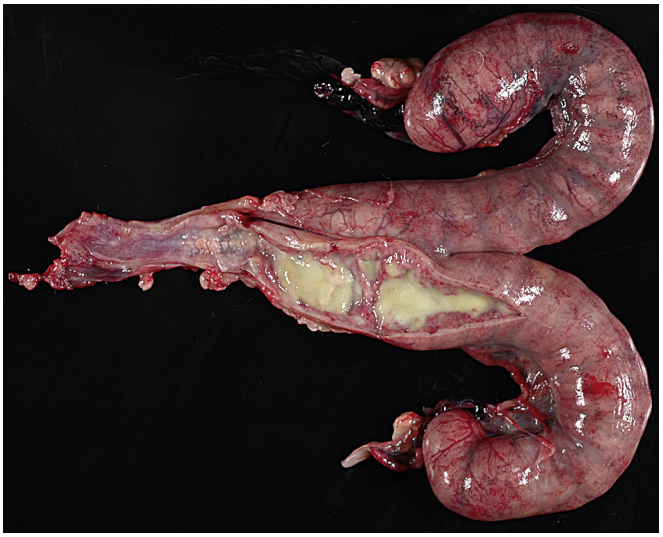

FIGURE 89-6 Uterus of an 11-year-old female spayed Pomeranian with pyometra after ovariohysterectomy. The uterine horns were severely dilated and fluid-filled. (Image courtesy University of California, Davis, Veterinary Anatomic Pathology Service.)

neoplasia.[46] Emphysematous pyometra has been reported in dogs but is uncommon.[47-49] Etiologic agents in emphysematous pyometra include *C. perfringens, Citrobacter diversus,* and *P. aeruginosa*.

In dogs, pyometra usually occurs in diestrus, but it can occur in anestrus. Middle-aged to older (mean age around 9 years), intact female dogs are most often affected, but pyometra has been reported in dogs as young as 8 months of age. Older dogs develop pyometra as a result of chronic, repeated exposure to progesterone with cycling over many years. In contrast, younger dogs tend to develop pyometra as a result of treatment of mismatings with estrogens. Pyometra is prevalent wherever routine ovariohysterectomy of dogs is not widely performed. In a study from Scandinavia, breeds of dogs with increased risk included collies, Rottweilers, Bernese mountain dogs, Cavalier King Charles spaniels, English cocker spaniels, and golden retrievers.[50,51] Nulliparous bitches are at increased risk for development of pyometra when compared with those that have had litters, but false pregnancy does not influence the risk for pyometra in dogs.

In cats, CEH also seems to underlie pyometra. Although cats with pyometra are generally more than 3 years of age (mean, 5 years), pyometra can occur in cats of any age.

Clinical Features

Clinical Signs

Clinical signs of pyometra in dogs usually occur 2 to 10 weeks after estrus or breeding, but occasionally occur as long as 15 weeks after estrus (mean, 7 weeks). In both dogs and cats, clinical signs may be acute or chronic and include lethargy, polyuria and polydipsia, vomiting, weight loss, inappetence, diarrhea, fever, and/or abdominal pain. Some dogs or cats show no signs of illness. Animals with *open-cervix pyometra*, the most common form of pyometra (>60% of dogs), usually have purulent vaginal discharge. The discharge may have a fetid odor and it may be mucopurulent, purulent, or contain blood. Dogs or cats with *closed-cervix pyometra* do not have vaginal discharge, but abdominal distention may be present. Animals with closed pyometra are more likely to have severe signs of systemic illness than those with open pyometra. Concurrent glomerular and tubulointerstitial disease and/or the effects of *E. coli* endotoxin may also contribute to signs of polyuria and polydipsia.[52,53] In some dogs or cats, pyometra is accompanied by severe sepsis or septic shock. When disease is severe the uterus can rupture, which leads to peritonitis.

Stump pyometra is an uncommon form of pyometra. It sometimes occurs after remnants of the ovaries are inadvertently left in place after ovariohysterectomy, but this is not always the case. Stump pyometra occurs most commonly in dogs, but has been reported in the cat.[54] Clinical signs are similar to animals with pyometra. Stump pyometras can also contribute to recurrent lower UTIs.

Physical Examination Findings

Purulent vaginal discharge, sometimes with a putrid odor, may be present in animals with bacterial vaginitis or open pyometra. Fever is most likely to be identified in animals with closed-cervix pyometra. Abdominal pain may be present on palpation of the abdomen. Abdominal palpation should always be performed cautiously when pyometra is suspected so that uterine rupture does not occur. Dogs and cats with severe pyometra may be lethargic, dehydrated, and show signs of severe sepsis or septic shock.

Diagnosis

Diagnosis of vaginitis, metritis, and pyometra is based on signalment, history, clinical signs, laboratory abnormalities, imaging findings, and, in some cases, bacterial culture of the urine or uterine contents obtained during surgery. Blind cystocentesis should never be performed if pyometra is suspected because of the risk of inadvertent puncture and rupture of the uterus. This also has the potential to occur with ultrasound-guided cystocentesis, but the risk is lower.

Laboratory Abnormalities

Acute metritis or pyometra (especially closed-cervix pyometra) may be associated with anemia, leukocytosis due to a neutrophilia, bandemia, a degenerate left shift, toxic neutrophils, and monocytosis. Thrombocytopenia and signs of organ dysfunction (such as azotemia, increased serum ALP activity, and coagulation abnormalities) may be detected in dogs with severe sepsis or septic shock. Azotemia may result from severe dehydration or concurrent pyelonephritis. Hypoalbuminemia and electrolyte abnormalities such as low serum sodium-to-potassium ratios may be present.[55,56] Dogs and cats with chronic pyometra can have few laboratory abnormalities; some animals are hyperglobulinemic. On urinalysis, abnormalities consistent with UTI may be present. Urine protein-to-creatinine ratios may be increased as a result of renal tubular or glomerular injury.[53]

Diagnostic Imaging

Plain Radiography

Abdominal radiographs in dogs with pyometra may reveal the presence of a large coiled or tubular mass in the caudal and mid-abdomen that displaces the small intestine cranially and dorsally. The uterus may not be visible in dogs with open pyometra. Differentiation of pyometra from pregnancy may require ultrasound examination. Localized or generalized loss of abdominal detail may be present in dogs with peritonitis secondary to uterine rupture.

Sonographic Findings

Ultrasound is the imaging technique of choice for diagnosis of pyometra and differentiation of pyometra from pregnancy. However, it may not effectively distinguish pyometra from mucometra or hydrometra. Dogs with pyometra have an enlarged uterus, which is immediately dorsal to the bladder. The uterus may be thin-walled and distended with echogenic intraluminal fluid, or have a thickened wall with anechoic areas due to glandular proliferation and enlargement.[57] Stump pyometra may be recognized as a hypoechoic structure that is located dorsal and caudal to the urinary bladder (Figure 89-7).

Microbiologic Tests

Isolation and Identification

Fine-needle aspiration of the uterus is contraindicated in animals with suspected pyometra because of the risk of uterine rupture. Instead, the bacteria involved in pyometra are initially identified through bacterial culture of the urine, which frequently contains the same bacteria as those involved in the pyometra. However, a negative urine culture does not rule out pyometra, and

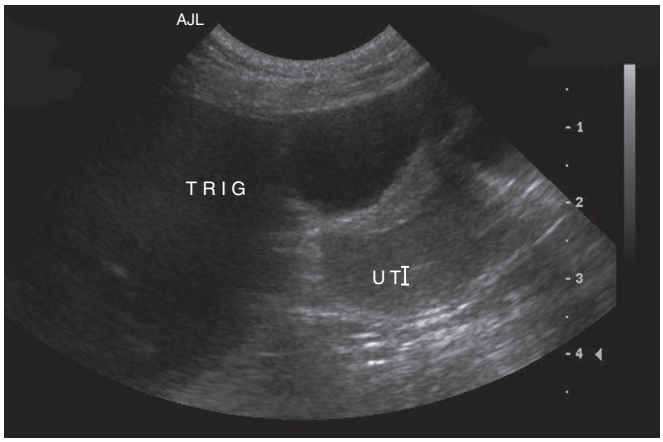

FIGURE 89-7 Ultrasound image of the urinary bladder and uterine stump in a 3-year-old female spayed mixed-breed dog that had vaginal discharge with a putrid odor due to a stump pyometra. An oval structure (*UT*) that contained flocculent material is present within the pelvic inlet caudal to and dorsal to the anechoic urinary bladder (*TRIG*, trigone). A cystic structure was seen in the region of the left ovary that represented a left ovarian remnant (not shown).

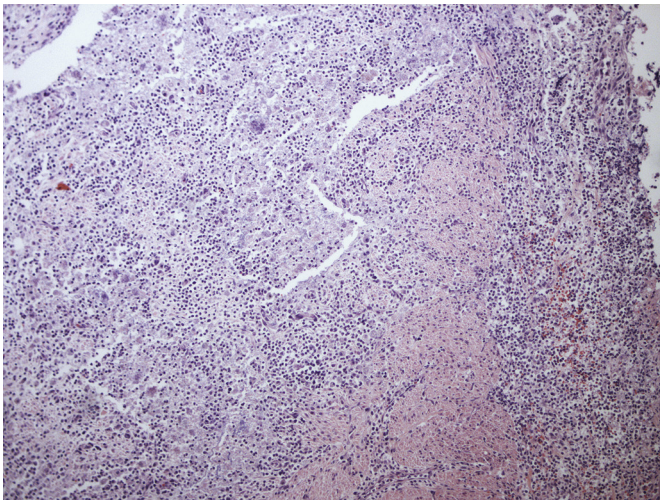

FIGURE 89-8 Histopathology of the uterus from a 7-year-old female poodle with pyometra. The dog was seen for vomiting, inappetence, obtundation, nystagmus, collapse, and abdominal distention. The owner elected euthanasia. Severe, chronic, suppurative metritis with uterine perforation and septic peritonitis was found at necropsy. The myometrium (pink) is almost completely replaced by large numbers of inflammatory cells. Aerobic and anaerobic bacterial culture of the abdominal fluid yielded mixed growth that consisted of *Escherichia coli* and a non-enteric gram-negative aerobic bacterial species, a *Bacteroides levii*–like anaerobe, *Bacteroides fragilis*, *Prevotella heparinolyticus*, *Fusobacterium nucleatum*, and *Peptostreptococcus anaerobius*. H&E stain.

occasionally the organisms isolated from the urine differ from those causing the pyometra. For animals with open pyometra, culture of a swab specimen collected from the cranial vaginal vault could be considered, but the bacteria cultured may or may not be the same as those present within the uterus. Tissues removed surgically can be submitted for culture and susceptibility testing. This should be performed despite administration of broad-spectrum antimicrobial drugs before surgery, because these drugs are unlikely to penetrate pus within the uterus. If possible, both anaerobic and aerobic bacterial cultures should be submitted. Blood cultures could be considered when signs of severe sepsis are present.

Pathologic Findings

As for other urogenital infections, acute pyometra is associated with a dense neutrophilic infiltrate on histopathology (Figure 89-8), and intralesional bacteria may be identified; chronic infections may be associated with histiocytic or lymphoplasmacytic infiltrates. CEH (expansion of the endometrium with hyperplastic and dilated or cystic glands) and corpora lutea may be identified.

Treatment and Prognosis

Sick dogs or cats with metritis or pyometra should be treated aggressively with intravenous fluids and broad-spectrum parenteral antimicrobial drugs that have activity against gram-negative bacteria and anaerobes, such as a combination of clindamycin or metronidazole and a fluoroquinolone. Ovariohysterectomy is strongly recommended for animals with pyometra and may need to be performed on an emergency basis to resolve sepsis or septic shock. Caution is required to avoid rupture of a distended or friable uterus during surgery, because this has been associated with an increase in mortality (from <10% to approximately 50%). Reevaluation should be performed 1 week after discharge from hospital and should include physical examination, a CBC, biochemistry panel, and urinalysis. Usually there is a rapid response to treatment and hematologic and biochemical abnormalities resolve within this time period. The white cell count can increase dramatically after surgery before it returns to normal, because of sudden removal of the leukocyte "sink". Antimicrobial drug treatment should be continued for 7 to 10 days after ovariohysterectomy.

In conjunction with antimicrobial drug treatment, medical treatment with natural or synthetic prostaglandin $F_2\alpha$ ($PGF_2\alpha$) is an alternative option to surgery, especially for dogs with open pyometra that are young (<6 years of age) and otherwise in good health (Table 89-4[58-60]). This treatment causes lysis of the corpora lutea with expulsion of uterine contents. Medical treatment for pyometra without surgery is not recommended for dogs that are systemically unwell, and the possibility of pregnancy must first be ruled out with ultrasound. Medical treatment is less attractive for dogs with closed pyometra because (1) it risks uterine rupture; (2) it is less effective than in dogs with open pyometra; and (3) dogs are often systemically unwell. Nevertheless, it has been used with success in some dogs with closed pyometra. Medical treatment is most

TABLE 89-4

Published Treatment Protocols for Medical Therapy of Pyometra in Dogs and Cats[58-60]

Drug	Dose
Natural $PGF_{2\alpha}$ (Lutalyse)	0.1 mg/kg SC once (day 1), 0.2 mg/kg SC once (day 2), 0.25 mg/kg SC q24h days 3 to 7
Aglepristone	10 mg/kg SC once on days 1, 2, and 7
Aglepristone and cloprostenol	Aglepristone: 10 mg/kg SC once on days 1, 2, and 8 Cloprostenol: 1 µg/kg SC for 5 days on days 3 through 7

likely to be successful in dogs in late diestrus (>5 weeks after the end of estrus). Improvement is generally not evident for at least 48 hours, and adverse reactions to $PGF_2\alpha$ are common and include restlessness, hypersalivation, panting, vocalization, vomiting, diarrhea, mydriasis, fever, and rarely, signs of shock. As a result, treatment should be given in the morning on an empty stomach, hospitalization and observation are recommended for at least 4 hours after the injection (or throughout the treatment period in dogs with closed pyometra), and the dose should be carefully calculated and appropriate for the product used. Walking dogs for 20 to 40 minutes after drug administration (while adverse effects occur) may lessen the adverse effects and promotes close observation.[58] The severity of signs tends to decrease with each injection administered. For dogs with closed pyometra, serial abdominal ultrasound examinations are recommended every 2 days during treatment to evaluate for evidence of peritonitis. $PGF_2\alpha$ can also be used to treat postpartum metritis.

Aglepristone, a progesterone receptor antagonist that is available in Europe, appears to be a safe and effective alternative to $PGF_2\alpha$ for treatment of pyometra in both dogs and cats.[59] Addition of low-dose cloprostenol (a synthetic $PGF_2\alpha$ derivative) to aglepristone in one study increased success rate in dogs with open pyometra from 60% to 84%.[60]

All dogs treated medically should be reevaluated 2 weeks after treatment. If signs of pyometra persist, culture of a swab specimen from the cranial vaginal vault could be performed to determine if resistance to antimicrobials is present, and treatment should be repeated a second time or surgery performed. The measurement of serum progesterone to monitor effective treatment is not necessary, because it does not change treatment recommendations. After successful treatment, the dog or cat should be bred at each subsequent cycle until pregnancy occurs. The chance that subsequent pregnancy will occur is over 80%, and the vast majority of dogs that respond go on to have more than one litter. Once the dog or cat is no longer required as a breeding animal, it should be neutered.

Prevention

Routine ovariohysterectomy reduces the risk of pyometra. Although stump pyometra can still occur in neutered animals, it is relatively rare. There is no known treatment for CEH. Use of estrogens to treat mismatings is not recommended.

CASE EXAMPLE

Signalment: "Molly", a 6-year-old female spayed shih tzu mix from Sacramento, CA

History: Molly was brought to the UC Davis VMTH for evaluation of recently diagnosed nephrolithiasis and hematuria. Three weeks previously, the owners had observed blood in Molly's urine. There had been no stranguria, polyuria, polydipsia, or change in the frequency of urination. They took her to their local veterinary clinic, where blood work was performed; her hematocrit was 56.5% and thrombocytopenia (86,000 platelets/µL) was present. A urine dipstick analysis revealed 2+ protein, a pH of 8, hematuria, and pyuria. Urine specific gravity was 1.014. Abdominal radiographs revealed a 3-cm opacity in the right renal pelvis that was consistent with a nephrolith (see Figure 89-2). The kidneys had a mildly irregular shape but were normal in size. Treatment with amoxicillin was initiated (23 mg/kg PO q12h for 10 days). Twelve days later, the dog was returned for dental prophylaxis. A CBC showed a hematocrit of 50% and persistent thrombocytopenia (51,000 platelets/µL). An abdominal ultrasound showed a 2.9-cm right renal pelvic nephrolith and a 7-mm left renal pelvic nephrolith. The kidneys were normal in size but had a mildly irregular shape. There was moderate thickening of the apical wall of the urinary bladder, with a small (4-mm) apical polyp. Moderate flocculent suspended debris was present within the urine and multiple sand-like calculi were present. All other organs evaluated were within normal limits. The dental procedure was canceled and Molly was referred for further evaluation.

Other Medical History: Molly had traveled frequently to Oregon and Nevada. She was fed a stone dissolution diet (Royal Canin Urinary SO), which had been prescribed 4 years ago when crystals were seen in her urine on urinalysis, as part of a wellness examination. She was also occasionally fed dog treats. She had been vaccinated using a 3-yearly protocol for canine distemper virus, canine adenovirus, canine parvovirus, and rabies; and yearly for *Bordetella bronchiseptica*, canine coronavirus, leptospirosis, and Lyme disease. Her last vaccination was more than 8 months previously. She was treated with imidacloprid and ivermectin for flea and heartworm prophylaxis, respectively, each month.

Physical Examination:

Body Weight: 10.8 kg.

General: Bright and alert, hydrated. T = 101.6°F (38.7°C), HR = 128 beats/min, RR = 32, mucous membranes pink and moist, CRT < 1 s.

Eyes, Ears, Nose, and Throat: Mild epiphora was present bilaterally and there was mild dental calculus and gingivitis. No other clinically significant abnormalities were detected.

Integument: The abdomen was clipped from the previous ultrasound examination with healing clipper wounds. There was a 1-cm ecchymosis on the ventral abdomen.

Musculoskeletal: Body condition score was 7/9. The dog was ambulatory with normal gait.

Genitourinary/Gastrointestinal: The dog had a soft and mildly painful abdomen on palpation. The urinary bladder was moderately sized. Rectal examination was unremarkable. There was no vulvar discharge and no evidence of perivulvar dermatitis. A slightly recessed vulva was present.

All Other Systems: No clinically significant findings.

Laboratory Findings:

CBC:

HCT 49.1% (40%-55%)
MCV 70.3 fL (65-75 fL)
MCHC 35.0 g/dL (33-36 g/dL)
nRBC 1/100 WBC

WBC 10,200 cells/μL (6000-13,000 cells/μL)
Neutrophils 7140 cells/μL (3000-10,500 cells/μL)
Band neutrophils 102 cells/μL
Lymphocytes 1632 cells/μL (1000-4000 cells/μL)
Monocytes 816 cells/μL (150-1200 cells/μL)
Platelets 12,000 platelets/μL (150,000-400,000 platelets/μL)
MPV 21.6 fL (7-13 fL)
Many macroplatelets were reported on smear evaluation.

Serum Chemistry Profile:
Sodium 148 mmol/L (145-154 mmol/L)
Potassium 4.0 mmol/L (3.6-5.3 mmol/L)
Chloride 111 mmol/L (108-118 mmol/L)
Bicarbonate 23 mmol/L (16-26 mmol/L)
Phosphorus 3.6 mg/dL (3.0-6.2 mg/dL)
Calcium 10.1 mg/dL (9.7-11.5 mg/dL)
BUN 12 mg/dL (5-21 mg/dL)
Creatinine 0.9 mg/dL (0.3-1.2 mg/dL)
Glucose 92 mg/dL (64-123 mg/dL)
Total protein 6.1 g/dL (5.4-7.6 g/dL)
Albumin 3.4 g/dL (3.0-4.4 g/dL)
Globulin 2.7 g/dL (1.8-3.9 g/dL)
ALT 42 U/L (19-67 U/L)
AST 16 U/L (19-42 U/L)
ALP 85 U/L (21-170 U/L)
Cholesterol 257 mg/dL (135-361 mg/dL)
Total bilirubin 0.1 mg/dL (0-0.2 mg/dL)

Urinalysis: SGr 1.013; pH 8.0, 2+ protein (SSA), 1+ bilirubin, 4+ hemoprotein, no glucose, no ketones, >100 WBC/HPF, 30-50 RBC/HPF, no crystals or casts, many rods, rafts of atypical transitional cells, many degenerated cells.

Coagulation Panel: PT 9.9 s (7.5-10.5 s), PTT 8.4 s (9.0-12.0 s), fibrinogen 395 mg/dL (90-255 mg/dL).

Microbiologic Testing: Direct smear of urine: Moderate numbers of gram-negative rods and gram-positive cocci were visualized.

Aerobic bacterial urine culture and susceptibility (cystocentesis specimen): 10^5 CFU/mL *Proteus mirabilis*, *Proteus mirabilis* (nonswarming strain), and *Enterococcus faecalis*. Both *Proteus* spp. were resistant to ampicillin (≥256 μg/mL) but susceptible to amoxicillin–clavulanic acid (4 μg/mL), cephalexin (8 μg/mL), chloramphenicol (≤16 μg/mL), enrofloxacin (≤1 μg/mL), tetracycline (64 μg/mL), and trimethoprim-sulfamethoxazole (≤4 μg/mL). The *E. faecalis* was susceptible to ampicillin, amoxicillin–clavulanic acid (≤2 μg/mL), chloramphenicol (≤16 μg/mL), enrofloxacin (≤1 μg/mL), and tetracycline (16 μg/mL).

Diagnosis: *Proteus mirabilis* and *Enterococcus faecalis* cystitis and suspected pyelonephritis with nephrolithiasis, with possible secondary immune-mediated thrombocytopenia.

Treatment: Molly was treated with enrofloxacin (7 mg/kg PO q24h). The following day her platelet count increased to 31,000 platelets/μL, and by day 3 of treatment it was 64,000 platelets/μL. After 7 days of treatment, a CBC showed a neutrophil count of 5700/μL and no band neutrophils, and the platelet count was 79,000 platelets/μL. A urine culture obtained by cystocentesis at this time showed 10^4 CFU/mL of *E. coli* and *E. faecalis*. The *E. coli* was resistant to ampicillin, cephalexin, enrofloxacin, tetracycline, and trimethoprim-sulfamethoxazole, but susceptible to amoxicillin–clavulanic acid (64 μg/mL). The susceptibility of the *E. faecalis* had not changed, with the exception that the MIC for tetracycline was 32 μg/mL. Treatment was changed to amoxicillin–clavulanic acid (23 mg/kg PO q12h). When reevaluated 3 weeks later, Molly had no clinical signs of illness. A CBC showed only mild thrombocytopenia (146,000 platelets/μL, with an MPV of 12.6 fL). However, bacteria and large numbers of white blood cells were still present in the urine sediment, the urine pH was 8.0, and *E. coli* with the same susceptibility pattern was again isolated from the urine. An extended panel showed susceptibility to amikacin (≤4 μg/mL) and imipenem-cilastatin (≤1 μg/mL), but resistance to cefazolin, cefoxitin, cefpodoxime, cephalothin, gentamicin, marbofloxacin, orbifloxacin, and ticarcillin–clavulanic acid. The dosage of clavulanic amoxicillin–clavulanic acid was increased to 23 mg/kg PO q8h. The diet was changed to a commercial urolith dissolution diet (Hill's s/d Canine Dissolution diet). After an additional month, urinalysis findings were unchanged and the same *E. coli* was again isolated from the urine. The platelet count was 244,000 platelets/μL and a biochemistry panel was unremarkable. Abdominal radiographs and ultrasound showed no evidence of nephrolithiasis, but multiple small, rounded mineral opacities were present in the region of the right ureter.

Antimicrobial drug treatment was ultimately changed to amikacin (15 mg/kg SC q24h) 2 weeks later because an *E. coli* was isolated that was resistant to clavulanic acid–amoxicillin. Kidney values were monitored every 2 weeks during amikacin treatment to evaluate for nephrotoxicity. The urine then became sterile, and ultrasound examination showed disappearance of all urinary calculi over a 2-month period, after which antimicrobial drug treatment was discontinued and the diet was changed to a maintenance diet. Because of the recessed vulva and the dog's excess body condition, a weight loss program was discussed with the owner. Molly was diagnosed with a subclinical *Enterobacter aerogenes* UTI 2 months later, which was broadly susceptible to antimicrobial drugs and treated with enrofloxacin. The platelet count was within the reference range. Further evaluation for underlying conditions predisposing to recurrent UTIs (contrast cystourethrography and cystoscopy), followed by vulvoplasty if no other abnormalities were detected, were offered to the owners but they declined further treatment and evaluation. The dog remained alive, untreated, and without clinical signs 4 years later, at which time CBC and biochemistry panel results were unremarkable but MDR *E. coli* was repeatedly isolated from the urine.

Comments: This is an interesting case of bacterial cystitis and pyelonephritis associated with struvite nephrolithiasis, and probable secondary immune-mediated thrombocytopenia. The struvite urolithiasis was likely secondary to the *P. mirabilis* infection, because *P. mirabilis* produces urease. Months of antimicrobial treatment were necessary because of bacterial sequestration within urinary calculi. This may have explained continued isolation of bacteria from the urine in the face of antimicrobial drug treatment, although ultimately resolution of the *E. coli* infection quickly followed the change in antimicrobial drug choice. Meropenem would have been another appropriate choice based on the susceptibility of the organism isolated, but its use in animals is controversial because it is an important

Continued

option for treatment of serious resistant bacterial infections in humans. Fortunately, dissolution of the nephroliths occurred in this case with antimicrobial and dietary therapy, and surgery to remove infected uroliths was not required. Continued UTIs were a likely sequela in this dog in the absence of successful identification and treatment of an underlying cause. Although treatment of the UTI was necessary during nephrolith dissolution, treatment of the subclinical *E. aerogenes* infection may not have been necessary.

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