REVIEW ARTICLE / PREGLEDNI ČLANAK

Urinary tract bacterial infections in small animal practice: clinical and epidemiological aspects

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Abstract

The urinary tract infection (UTI) is a common disease in dogs and cats, and it can occur as isolated infections or recurrently. Recurrent cases are particularly common in cases with underlying health conditions. The diagnosis of UTIs in dogs and cats generally involves an integrated interpretation of clinical signs, urinalysis, and bacterial cultures. Diagnostic imaging can also help assessing or discarding anatomical lesions. One of the many microorganisms that can cause UTIs is *Escherichia coli*. Females, geriatric patients, and animals with comorbidities usually have an increased risk of UTI. Antimicrobial prescription is common for the treatment of UTIs in companion animals. However, nowadays, there is a growing concern about antimicrobial resistance due to over-prescription driving selection for resistance. Therefore, correct prescription and appropriate patient management are essential. This review aims to provide a summary of the clinical and epidemiological aspects of UTIs, contributing to improving veterinary practices and antibiotic prescription in the context of UTIs in companion animals.

Key words: *Cats; Clinical signs; Dogs; Epidemiology; Urinary tract infections*

Introduction

Urinary tract infections (UTIs) occur frequently in veterinary practice and are among the most common reasons for antibiotic prescription (Sykes and Westropp, 2014; Hernando et al., 2021). A wide variety of pathogens can cause UTIs, even though bacteria are the most frequent (Olin and Bartges, 2015; Kocúreková et al., 2021). These agents may cause a lower UTI, affecting the bladder (cystitis) and/or the urethra (urethritis); or upper TI, affecting renal pelvis (pyelonephritis) and/or ureters (ureteritis) (Kogika and Waki, 2015; Olin and Bartges, 2015; Teh, 2022). In some cases, bacterial agents may also colonize surrounding tissues, such as the

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prostate (prostatitis) or vagina (vaginitis) (Olin and Bartges, 2015; Kocúreková et al., 2021). In some cases, animals may reveal no clinical signs or mild discomfort while urinating, leading to signs of dysuria and pollakiuria that usually disappear with pharmacological treatment. Nevertheless, in severe cases, intravenous fluids, hospitalization, or surgery may be necessary (Weese et al., 2019).

Frequently, an etiological diagnosis is not performed due to financial constraints of the owner (Fonseca et al., 2021), and the empirical treatment antibiotic is initiated. Notwithstanding, antimicrobial drug treatment without knowing the responsible agent may lead to recurrent infection and treatment failure (Sykes and Westropp, 2014). Improper therapy has consequences for the patient (e.g., prolonged pain), economic concerns for the owner (as additional costs) and a public health impact (as the possibility of zoonotic transmission of resistant bacteria) (Weese et al., 2019; Yudhanto et al., 2022).

Previous studies have described patterns of antimicrobial prescriptions in companion animals in different countries. In this review, the 2019 ISCAID (International Society for Companion Animal Infectious Diseases) guidelines have been considered. Our aim is providing a brief review about the clinical and epidemiological aspects of UTIs, to improve veterinary practices, especially in antibiotic treatment.

Etiology of Urinary Tract Infections (UTIs)

The urinary tract (UT) is sterile, with the exception of the distal urethra and external genitalia, where commensal microbiota is present (Lanzi et al., 2022). In a few words, UTIs are more often caused by agents that belong to this microbiota or to the intestine's commensal microbiota (ascending infection) (Rodriguez, 2016) (Figure 1). Less commonly, an infectious agent can reach the UT from the kidney, through a descending route or, in other words, via hematogenous spread (Littman, 2011; Sykes and Westropp, 2014). Basically, for a UTI, two conditions must occur: 1) temporary or permanent failure in host's immunity, and 2) pathogens must be present in sufficient quantity and with specific virulence (Kogika and Waki, 2015; Kocúreková et al., 2021).

A wide variety of infectious agents can cause UTIs. Fungal infections, including *Candida* spp., have been described in cases of immunosuppression, chronic UT conditions, and animals receiving concomitant antibiotic therapy (Reagan et al., 2019; Dowling, 2023). However, recent data reported that viral, fungal, and parasitic infections represent less than 1% of UTIs cases (Kogika and Waki, 2015; Dorsch et al., 2019).

In general, UTIs bacterial agents are similar between the two species in small animal practice (Labato, 2009). *Escherichia coli* (*E. coli*) is the most frequently isolated agent in canines, felines, and even humans (Kocúreková et al., 2021; Weese et al., 2019), representing 33-55% of the isolated pathogens (Lima et al., 2021; DiBartola and Westropp, 2023). Bacteria such as *Enterococcus* spp., *Staphylococcus* spp., *Streptococcus* spp., *Enterobacter* spp., *Proteus* spp., *Klebsiella* spp., *Pseudomonas* spp., *Pasteurella* spp., and *Corynebacterium* spp. are also commonly isolated (Sykes and Westropp, 2014; Byron, 2019; Lanzi et al., 2022). UTIs usually involve a single microorganism. However, mixed infections, with two or more microorganisms, may also be involved (Nelson and Couto, 2009). According to Smee, (2020), 75% of dog isolates are single bacteria, 20% are caused by a combination of two species, and 5% by three or more species. A similar frequency was found for cat patients (Pressler and Bartges, 2010). Mixed infections are more frequent cases of prolonged use of urinary catheters or other comorbidities (Dorsch et al., 2016).

Epidemiology

Bacterial UTIs are estimated to affect about 14% to 15% of dogs over their lifetime (Dowling, 2023; Rodriguez, 2016). Females are more affected (Furini et al., 2013; Hall et al., 2013; Lima et al., 2021), with a higher prevalence in spayed and matured animals (7 to 8 years old) (Sykes and Westropp, 2014; Lanzi et al., 2022; Llido et al., 2020).

In cats, lower UT diseases are normally approached as a disease complex, called the feline lower UT disease (FLUD). Idiopathic cystitis and UT inflammatory disease without the presence of an infectious agent, is far more than bacterial UTIs in this species (Kovarikova, 2020; Heseltine, 2022). In fact, according to Rodriguez (2016) and Heseltine (2022), less than 10% of cats with urinary clinical signs have a positive urine culture. Unlike dogs, cats seem to have an innate resistance to bacteria (Bartges, 2012). Nevertheless, similarly to dogs, positive urine cultures are more easily found in female cats. The incidence tends to increase with age, and it is especially higher after 10 years old (Dorsch et al., 2019; Kovarikova et al., 2020; Leckcharoensuk et al., 2001), neutered females and/or in cases with comorbidities (DiBartola and Westropp, 2023). Studies performed by Sævik et al. (2011) in Norway have also shown a predisposition in purebred cats, being the Abyssinian (Gerber, 2007; Dorsch et al., 2019) and the Persian breeds the most susceptible (Sykes and Westropp, 2014).

Pathogenesis

In ascending infections, the resident microbiota present in the distal urethra, genitalia (Figure 1), and in the intestine become causes of disease (Rodriguez, 2016; Lanzi et al., 2022). Several studies have shown that, in dogs, at the time of infection, the pathogens which colonize the urinary bladder are the same that are predominant in the gastrointestinal tract (Low et al., 1988; Ball et al., 2008; Johnson et al., 2008). Although infrequent, UTIs can also occur through hematogenous spread. Provenances of these bacteria bacterial endocarditis or extension from infected tissues surrounding the UT, such as prostate gland (Smee et al., 2013a; DiBartola and Westropp, 2023).

Natural Host Defense Mechanism

Non-pathogenic bacteria in a normal animal can become pathogenic in immunosuppressed patients (Pressler and Bartges, 2010). The development of UTI depends on the balance between the host's defense mechanisms and the virulence factors of the pathogen (Dorsch et al., 2019; Kovarikova et al., 2020).

Normal urine storage and voiding

The mechanical and unidirectional elimination that occurs in normal urination is responsible for eliminating 95% of non-adherent bacteria that reach the urinary bladder (DiBartola and Westropp, 2023). Complete emptying of the urinary bladder minimizes the agent's exposure time, reducing the probability of colonization (Teh, 2022; DiBartola and Westropp, 2023). Urinary obstruction (tumors, hypertrophic lesions, or urethral stenosis) as well as incomplete emptying of the urinary bladder (due to spinal cord injury or congenital/acquired bladder atony) increases bacterial proliferation and consequent infections (Smee et al., 2013; Teh, 2022).

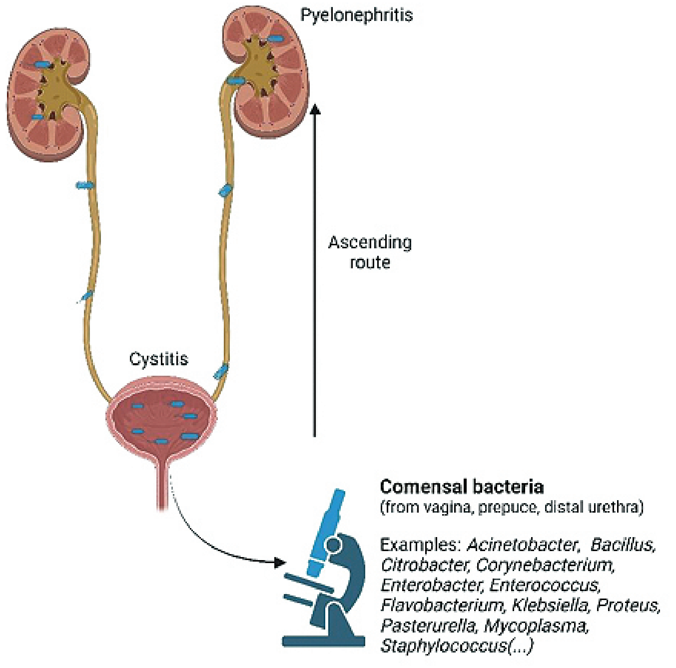

Figure 1. Pathogenesis of ascending UTIs (Created with Biorender.com)

Dogs with intervertebral disc disease often present urinary retention and abnormal urination, conditions that predispose them to UTI (Baigi et al., 2017; Teh, 2022). Studies have shown that 38% of dogs undergoing spinal disc surgery develop UTI within three postoperative months (Olby et al., 2010). Moreover, the presence of bacteriuria has also been documented in 74% of dogs paralyzed for more than three months (Baigi et al., 2017).

Antimicrobial properties of urine

The combination of a low pH, high concentrations of urea and organic acids, and higher osmolarity makes the UT inhospitable for bacterial growth (Teh, 2022). According to several authors, animals with more diluted urine are more susceptible to bacterial growth (Senior, 2007; Litster et al., 2009; Ruzafa et al., 2012). However, these results do not seem consistent with other studies (Baillif et al., 2008; Dorsch et al., 2019; DiBartola and Westropp, 2023). A study conducted by Teh (2022) also found a higher prevalence of UTI in dogs that received diuretics.

Anatomic structures

The high pressure and the peristaltic contractions at the level of the urethra, help prevent the ascent of commensal bacteria (Teh, 2022; DiBartola and Westropp, 2023). The length of the urethra and prostatic secretions in males contribute to a lower incidence of UTI in male dogs (Smee, 2020). The vesicoureteral valve, created by the oblique passage of the ureters through the bladder wall, prevents vesicoureteral reflux (Confer and Panciera, 1998; Teh, 2022). Congenital or acquired abnormalities, such as ectopic ureters, are associated with ascending UTIs, especially pyelonephritis (Smee et al., 2013a). Furthermore, persistent urachus is associated with chronic UTI, and hypoplasia or vulvar atresia is related to recurrent UTIs (Lightner et al., 2001; Smee, 2020). Animals undergoing urethrostomy often present chronic UTIs (Senior, 2007, Kogika and Waki, 2015). Additionally, the presence of skin folds near the vulva often results in located dermatitis, which increases the likelihood of bacterial ascent through the urethra. Episioplasty (excision of skin folds) in animals with this dermatitis usually solves the clinical signs of chronic UTI (Lightner et al., 2001).

Mucosal defense barriers

The UT has several defense mechanisms. The commensal microbiota occupies most of the epithelial receptors, produces bacteriocins, and competes for the same nutrients as pathogenic bacteria (Kogika and Waki, 2015; DiBartola and Westropp, 2023). The epithelial cells in the bladder form an impermeable barrier. In case of infection, bacteria can induce cellular apoptosis, resulting in the exfoliation of these cells (Smee et al., 2013a). Moreover, the urothelium produces and releases glycosaminoglycans (GAGs) and proteoglycans, which prevent the adherence of pathogens and crystals to the epithelium (Smee, 2020). As well as the local production of Immunoglobulins A and G (IgA, IgG) (Kogika and Waki, 2015; Teh, 2022; DiBartola and Westropp, 2023). Thus, mucosal injury due to urolithiasis, catheterization trauma, neoplasia, or cyclophosphamide-induced injury induces secondary UTI (Kogika and Waki, 2015; Smee, 2020). A previous study suggests that ovariectomized animals may have a higher risk of UTI because the amount of GAG produced is lower (Senior, 2011). In a study conducted by Budreckis et al. (2015), 55% of dogs with transitional cell carcinoma showed positive urine cultures.

Local and systemic immune competence

Immunosuppressive conditions, such as chronic kidney disease (CKD), *diabetes mellitus* (DM), hyperadrenocorticism (HD), hyperthyroidism (HT) and a prolonged administration of corticosteroids (CE), have been related to UTI (Hall et al., 2013; Smee, 2020). In addition to immunosuppression, glycosuria and low urinary osmolality are associated with some of these conditions, which also increase the susceptibility to UTIs (Teh, 2022).

A retrospective study involving 101 dogs with DM, HD, or both concluded that 41.6% developed UTI (Smee et al., 2013a). Another retrospective study in cats reported bacterial UTI in 17-30% of cats with CKD, 12-13% with DM, and 12-22% with HT (Smee et al., 2013a). Mayer et al. (2007) and Baillif et al. (2008) found positive cultures in 17% and 22% of cats with CKD and 22% and 12% with HT, respectively. Dogs treated with immunosuppressive drugs for long periods showed a high prevalence of positive urine cultures (Torres et al., 2005; Senior, 2007).

Microbial factors

UTI leads to the expression of microbial virulence factors (VF), which are responsible for adherence, colonization, and invasion in the urinary tissue (Kogika and Waki, 2015; Dorsch et al., 2019; Raheema, 2021). For example, *Proteus* spp., *C. urealyticum, Staphylococcus* spp., and *Klebsiella* spp. can hydrolyze urease, converting it into ammonia (Senior, 2011). This compound not only induces direct damage to the epithelium but also facilitates bacterial invasion and its persistence (Litster et al., 2011; Byron, 2019), as it increases pH and promotes crystalluria (Litster et al., 2011). Other species have intrinsic mobility and can undergo retrograde migration, i.e., against the urinary flow (Senior, 2006), while others can thrive in hypertonic environments such as the renal medulla and bladder where leukocyte migration and phagocytosis are compromised (Nelson and Couto, 2009). Some enzymes, like beta-lactamases, allow them to resist the action of antimicrobials such as penicillins and cephalosporins (Kogika and Waki, 2015). *E. coli* presents a high number of virulence factors (Tramuta et al., 2011; Kern et al., 2018; Gunathilake et al., 2023; Liang et al., 2023).

Clinical signs

The clinical signs depend on the site of infection, duration of disease, presence or absence of predisposing causes, compensatory response of the animal, virulence, and the quantity of uropathogenic agents (Smee, 2020). Inflammation of the lower UT often results in polyuria, stranguria, dysuria, inappropriate urination, and hematuria (Dorsch et al., 2019; Smee, 2020). Pain, retention, or even urinary incontinence may arise because of vesicourethral inflammation (Senior, 2011; Rodriguez, 2016). Animals with involvement of the upper UT may present polyuria, polydipsia, pain in the lumbodorsal region, vomiting, hyperthermia, lethargy, and anorexia (Rodriguez, 2016).

Diagnosis

Clinical signs of UTI are not specific or pathognomonic (Hernando et al., 2021). On the other hand, distinguishing bacterial from idiopathic cystitis or subclinical bacteriuria represents a challenge. A complete urinalysis with a positive culture is crucial for a reliable diagnostic (Dorsh et al., 2019).

Urinalysis is an important clinical diagnostic tool in these patients (Yadav et al., 2020). The physical properties of urine (color, odor, turbidity, and density) should be evaluated and interpreted macroscopically (Smee et al., 2013b; Yadav et al., 2020). Chemical properties can be assessed using urine test strips, providing information such as pH (whose value changes in the presence of urease-positive bacteria) (Nelson and Couto, 2009), the presence of blood, protein, and glucose (Yadav et al., 2020). A recent study by Farris et al. (2022) reported that leukocytes in urine strips predicts pyuria, but nitrites do not confirm infection. Examination of the sediment allows the determination of the presence of epithelial cells, red blood cells (hematuria), inflammatory cells (pyuria), and/or bacteria (Smee et al., 2013b; Yadav et al., 2020). In the presence of bacteriuria, Gram staining may be advantageous (Soares et al., 2024). Bacteriuria has moderate sensitivity and high specificity in predicting bacterial growth, but this relationship decreases in urines with low urinary densities (urine specific gravity (USG) ≤1.012) (Torre et al., 2022). Therefore, isosthenuric or hyposthenuric urines should always be subjected to culture (Rodriguez, 2016). The presence of hematuria, pyuria, and proteinuria may indicate UTI, but not its cause or location (Lloyd, 1987; DiBartola and Westropp, 2023). Therefore, ideally, urine should be subjected to a microbiological culture in aerobic conditions before treatment to confirm the presence and type of bacteria (Pressler and Bartges, 2010; Smee et al., 2013b; Dorsch et al., 2019; Lanzi et al., 2022; Lien and Wang, 2023). Cultures in anaerobic conditions are only necessary when there is a suspicion of emphysematous cystitis (Littman, 2011). Recent and promising studies have utilized rapid immunoassay tests (RIA; Rapid Bac) to detect bacteriuria, showing high specificity and sensitivity. Moreover, it represents an inexpensive, fast, and easyto-perform technique (Grant et al., 2021; Sutter et al., 2023).

Urine collection for culture should, whenever possible, be performed by cystocentesis to prevent contamination by bacteria inhabiting the distal urethra, prepuce, or vulva (DiBartola and Westropp, 2023). Other collection methods (catheterization or spontaneous micturition) should only be used when cystocentesis is contraindicated (e.g., suspicion of transitional cell carcinoma of the bladder or pyoderma on the ventral abdomen) (Smee et al., 2013b) or when it is not feasible (animals with severe clinical signs of UTI) (Pressler and Bartges, 2010). Van Duijkeren et al. (2004) demonstrated that while urine culture was negative in 79% of samples collected by cystocentesis, this value decreased to 55% when collected by catheterization, and only 17% when collected by midstream voiding.

Diagnostic imaging (radiography, ultrasound, or cystoscopy) can help finding concomitant lesions (Mazda et al., 2022). Figure 2 summarizes the general diagnostic approach to UTIs.

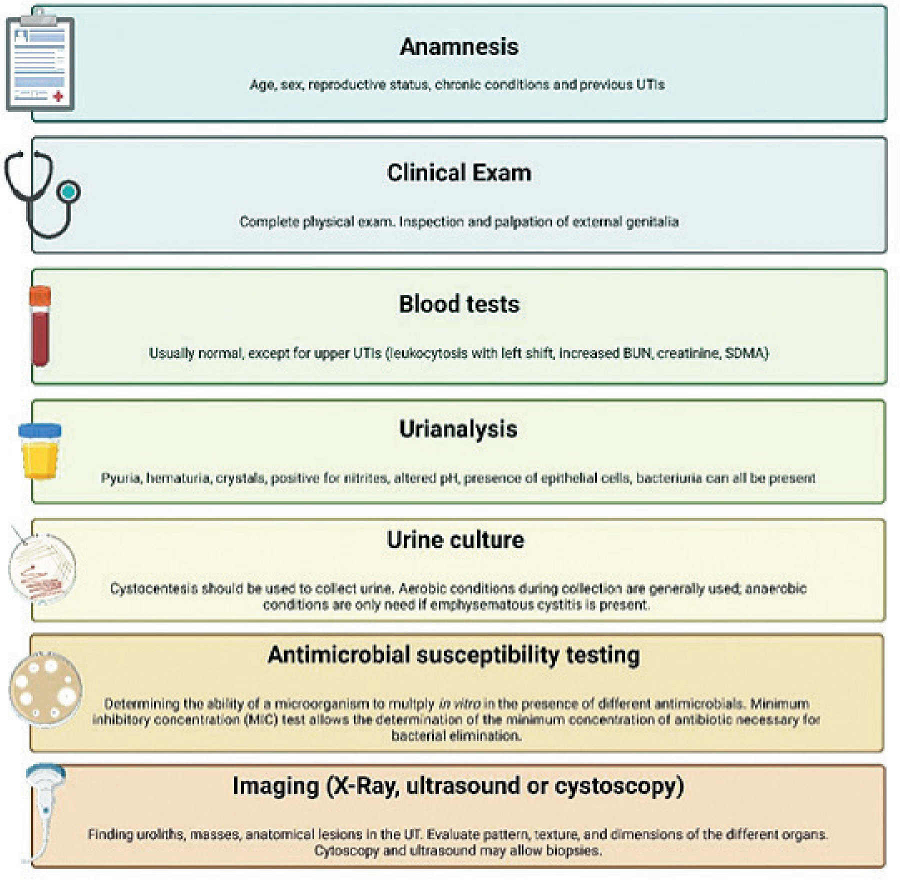

Figure 2. Diagnostic methods when approaching UTIs. Created with Biorender.com. (Pressler and Bartges 2010; Littman 2011; Papich 2013; Richter et al., 2019; Weese et al., 2019; Llido et al., 2020; Lanzi et al., 2022; Lien and Wang, 2023)

Treatment

Treating UTIs in dogs and cats requires a comprehensive approach, including appropriate antibiotics, addressing underlying causes, and providing supportive care (Sykes and Westropp, 2014). A retrospective study in dogs shows that the prescription of antibiotics is not usually preceded by proper diagnostic testing, potentially leading to over-treatment with antibiotics (Sørensen et al., 2018). The empirical treatment and the overuse (or misuse) of antibiotics may promote selection pressure and the emergence of resistant bacteria (Schwarz et al., 2017; McEwen and Collignon, 2018; Richter et al., 2020). In fact, a single dose of antibiotic can be sufficient for an entire bacterial population to gain resistance (Nelson and Couto, 2009). The risk is more significant as the number of antibiotics used increases (McEwen and Collignon, 2018). Currently, numerous studies demonstrate the transmission of microorganisms and multidrug-resistant (MDR) strains between humans and their companion animals (Johnson & Clabots 2006; Eggertsdóttir et al., 2007; Johnson et al., 2008; Pomba et al., 2017; Schwarz et al., 2017; Derakhshandeh et al., 2018; Fernandes et al., 2018; Grönthal, et al., 2018; Rampacci et al., 2018; Belas et al., 2021). Table 1 summarizes the reasons for antibiotic treatment failure.

The UT of dogs is the most common extraintestinal site to find MDR *E. coli* and *Enterobacter* spp. with 62% and 58% of isolates, respectively (Smee et al., 2013b; Hutton et al., 2018). In a multicenter study in Europe conducted by Marques et al. (2016), it was found that Southern countries had higher levels of resistance to antibiotics for all urinary bacteria compared to Northern countries. Moreover, the prevalence of multidrug-resistant *E. coli* was also higher in these countries. Studies in Australia (Scarborough et al., 2020), Africa (Qekwana et al., 2018), central Italy (Smoglica et al., 2022), the United Kingdom (Fonseca et al., 2021), and even Portugal (Garcês et al., 2022) have found increasingly higher prevalences of MDR *E. coli.*

Because of this phenomenon, the World Health Organization (WHO) has classified antimicrobials based on their importance in human medicine (McEwen and Collignon, 2018), and it restricted the

Table 1. Problems and reasons for the antimicrobial failure.

Type	Reason	References
Pharmacokinetics	The chosen antibiotic, dosage, or the duration of treatment. Drugs' interactions. The drug does not reach sufficient concentrations in the urine. Antibacterial drug resistance	Barsanti, 2009; Papich, 2013; Foster, 2017
Diagnosis	Incorrect diagnosis	Papich, 2013
Intrinsic complications	Bacteria are protected from the action of the antibiotic in the. renal tissue, the prostate gland, or even within the matrix of urinary calculi or in a biofilm	Thompson et al., 2011
Immunological status	Depressed patient immunologic status. Inability to identify and eradicate predisposing factors and underlying conditions.	Papich, 2013
Practical issues	Poor owner compliance	Foster, 2017

treatment options in veterinary medicine. Antimicrobials such as third generation cephalosporins, carbapenems, and fluoroquinolones should not be used in veterinary medicine or only used under rare circumstances (Dorsh et al., 2019; McEwen and Collignon, 2018). The chosen antimicrobial agent should be based on susceptibility testing of uropathogen (Olin and Bartges, 2015). When this is not possible, the empirical treatment should be based on the variation in bacterial prevalence rates and antimicrobial resistance patterns across different regions (consulting guidelines studies, local studies, national databases, or surveillance systems (McEwen and Collignon, 2018; Hernando, 2021).

Classification of UT infection and its clinical management

Sporadic bacterial cystitis

In a healthy animal, i.e. patients with normal anatomy and without associated comorbidities, sporadic bacterial infections are more frequent. The occurrence of three or more episodes in a year excludes a bladder infection from this group (DiBartola and Westropp, 2023; Weese et al., 2019). Diagnosis is based on clinical signs compatible with UTI, urinalysis (pyuria and bacteriuria increase suspicion of infection), and urine culture with an antibiotic susceptibility test (AST) (Weese et al., 2019). Nonsteroidal anti-inflammatory drugs (NSAIDs) (such as carprofen, ketoprofen, meloxicam, piroxicam and robenacoxib) or tramadol may be initiated for three to four days to minimize the animal's discomfort until a microbiological result is obtained (He et al., 2022; Sykes and Westropp 2014).

Empirical antimicrobial treatment can be initiated, especially in animals with clinical signs and no previous antibiotics exposure. However, empirically antibiotherapy should be adjusted to the type of pathogen and resistance patterns (Weese et al., 2011). Amoxicillin (11-15 mg/kg orally every 8 hours) or trimethoprim sulfamethoxazole (15 mg/kg orally every 12 hours) can be used as a first-line antibiotic therapy (DiBartola and Westropp, 2023). The guidelines proposed by ISCAID recommend a short-term therapy of 3 to 5 days in dogs and cats, as in humans (Weese et al., 2019). The antibiotic should not be changed if there is a clinical improvement, even if antimicrobial susceptibility testing indicates resistance (Weese et al., 2019). If there is no clinical response within 48 hours, clinicians should look for factors that can be impairing antimicrobial's effectiveness, before changing the antibiotic (DiBartola and Westropp, 2023).

Recurrent bacterial cystitis

Animals that have three or more episodes of bacterial cystitis within a year, or at least two in the past six months are included in this group. Recurrent infections may result from relapse, persistent infection, re-infection, super-infection, as summarized in Table 2.

Recurrent infections have been reported in 0.3% of hospitalized dogs, with spayed females being the most represented for this type of infection (Teh, 2022). Microorganisms such as *Enterococcus* spp. and *Pseudomonas* spp. are rarely found in sporadic cystitis, but their prevalence increases in animals with recurrent UTIs (Thompson et al., 2011). Diagnosis should always be based on urine culture. Furthermore, searching for underlying causes is imperative, especially if the identified pathogen differs from the initial one (Weese et al., 2029). In severe cases, empirical treatment can be started and should follow the lines of sporadic cystitis. Regardless of the AST result, the anti-

Table 2. Causes of infection in recurrent bacterial cystitis.

Causes of Infection	Description	Clinical Signs	Reference
Relapse	Infections caused by the same species of bacteria as the initial infection. Clinical signs quickly return after discontinuation of antimicrobial treatment. The antimicrobial was ineffective in eliminating the microorganism.	Quick return of clinical signs	Weese et al., 2011; Dorsch et al., 2019; DiBartola and Westropp, 2023
Persistent Infection	Bacteria that caused the infection remain present during and after therapy.	Presence of bacteria during and after therapy	Dorsch et al., 2019
Reinfection	Recurrent infections caused by a different bacterial agent from the one that caused the primary infection. Previous antibacterial treatment was effective in the first infection, but the UT was infected by another bacteria. It suggests no elimination of predisposing factors, multiple pathogens, iatrogenic infection, or spontaneous reinfection.	Recurrent infections with a different bacterial agent	Lloyd, 1987 Weese et al., 2011; Kogika and Waki, 2015; Dorsch et al., 2019; DiBartola and Westropp, 2023
Superinfection	Appearance of a new infection during another infection. The new microorganism differs from the one that caused the previous infection.	New infection during an existing infection	Dorsch et al., 2019

biotic is only changed if there is no clinical response to empirical treatment. A short-term treatment (3-5 days) is suggested, mainly if it is a reinfection. Longer treatments (7-14 days) are only recommended for persistent or recurrent infections, and when there are anatomical lesions (Weese et al., 2019).

For long-term treatments, urine cultures should be done 5-7 days after the day 1, and 5-7 days after the end of the treatment. When urine cultures are positive, predisposing factors and associated comorbidities should be investigated before the antibiotic is changed. The presence of bacteriuria in an animal without clinical signs should be treated as subclinical bacteriuria, as discussed in the next section (Weese et al., 2019).

Subclinical bacteriuria

If the animal shows a positive urine culture without clinical signs, it should be diagnosed as subclinical bacteriuria. The prevalence of this is low (2-12%) in healthy dogs, but increases to 15-74% in obese animals or in presence of comorbidities (Eggertsdóttir et al., 2011; O`Neil et al., 2013; McGhie et al, 2014; Olin and Bartges, 2015). In cats, this prevalence appears to be lower than in dogs (Puchot et al., 2017), and it is higher in matured and geriatric females (DiBartola and Westropp, 2023).

The presence of bacteria and inflammatory cells in urinary sediment does not always indicate UTI. Therefore, the diagnosis of subclinical bacteriuria should be based on urine culture (Lien and Wang, 2023; O'Neil et al., 2013; McGhie et al., 2014; Weese et al., 2019; Torre et al., 2022). For both species, DM (McGuire et al., 2002; Bailiff et al., 2006; Nelson et al., 2023) as well as long-term administration of corticosteroids (Torres et al., 2005) were predisposing factors for subclinical bacteriuria. Baigi et al. (2017) found similar results in chronically paralyzed dogs. The same happened for White et al. (2013) for cats with chronic kidney disease. Moreover, Harrer et al. (2022) found a high prevalence of positive urine cultures in animals receiving antineoplastic drugs. In contrast, Peterson et al. (2020) did not observe a relationship between positive urine culture and hyperthyroidism in cats. Notwithstanding, ISCAID generally advises against performing urine cultures in animals without clinical signs of UTI, unless there are particular comorbidities.

The bacterial strains involved in subclinical bacteriuria often have few virulence factors or low bacterial counts (Smee et al., 2013b). Treating subclinical bacteriuria cases with low bacterial counts can contribute to antibiotic resistance and may result in secondary colonization by more pathogenic strains. Moreover, the treatment of bacteriuria in humans has been questioned due to the induced resistance, and because it is normally ineffective (Dorsch et al., 2019; Freitag, 2011). According to Weese et al. (2019), treatment of subclinical bacteriuria in veterinary medicine should only be performed in three situations: (a) when there is a high risk of bacterial ascension or systemic infection (e.g., immunocompromised patients, renal abnormalities), (b) animals that are subjected to surgical or endoscopic procedures of the UT, (c) when the bladder is secondary infected by extra-UT bacteria (Weese et al., 2011; Westropp et al., 2011; Dorsch et al., 2019).

Pyelonephritis

Most pyelonephritis are caused by Enterobacteriaceae, ascending from the lower UT (Wong et al., 2015). Diagnosis is based on clinical signs, blood and urine tests, and diagnostic imaging (William et al., 2004; DiBartola and Westropp, 2023). Pyelocentesis for cytology and urine culture should be considered when cystocentesis results are negative. Blood cultures should be performed whenever there is a suspicion of bacteremia (Weese et al., 2019; DiBartola and Westropp, 2023). In acute situations, patient hospitalization is usually necessary for parenteral antibiotherapy (Pressler and Bartges, 2010). In most cases, fluoroquinolones (which are effective to Enterobacteriacea) should be administered (Weese et al., 2019; DiBartola and Westropp, 2023). According to ISCAID, 10-14 days of treatment are recommended and there is no indication that extended treatment is more effective (Weese et al., 2019). If there is clinical failure after 72 hours of treatment, predisposing causes should be investigated. However, if there is a clinical improvement with a microbiological failure, clinicians should suspect of subclinical bacteriuria (Weese et al., 2019). Nevertheless, in most cases, complete re-evaluation of the animal with clinical examination, laboratory tests, and urine culture should be performed 1-2 weeks after initial antibiotic treatment.

The presence of a complicated cystitis (e.g. emphysematous, encrusting, or polypoid) usually requires a more aggressive treatment, which means long-term antibiotic therapy and surgical interventions (Dorsch et al., 2019; Weese et al., 2019). Emphysematous cystitis is usually associated with *E. coli* infections (due to glucose fermentation) and frequently occurs in animals with DM (DiBartola and Westropp, 2023). Encrusted cystitis is normally caused by urease-positive bacteria such as

Corynebacterium urealyticum are isolated, leading to the precipitation of crystals and the formation of crusty plaques on the bladder mucosa (DiBartola and Westropp, 2023). Cystitis with polypoid proliferations of the bladder mucosa is associated with *Proteus* spp. (Dorsch et al., 2019).

Prevention and prophylaxis

Although a few scientific studies have measured their efficacy, the use of adjuvant therapies can be considered in order to avoid a management of UTIs exclusively dependent on antibiotics. As an illustration, the use of urinary acidifiers (Nelson and Couto, 2009); or urinary antiseptics such as methenamine (Weese et al., 2019; Olin and Bartges, 2015) has been suggested for this purpose. In women, intentional vaginal colonization by lactic acid-producing bacteria is associated with a reduction in the frequency of UTIs. However, Hutchins et al. (2013) found no effectiveness of this substance in female dogs. Growing studies with cranberry extracts, glycosaminoglycans, and vaccines against bacterial fimbriae seem to reduce bacterial adhesion to the uroepithelium in humans. However, further studies are required in companion animals (Bartges, 2012; Weese et al., 2019). The use of estrogens as a preventive therapy has been suggested in female dogs with recurrent vagino-cystitis (Bartges, 2012). More recently, live biotherapeutic products seem to be promising in the treatment of recurrent cystitis in dogs, even though more studies are necessary (Segev et al., 2018; Nelson et al., 2023).

Due to the increasing number of antibiotic-resistant UT infections, preventive measures have a crucial role nowadays. Weese et al. (2019) suggested some guidelines for managing catheterized animals and performing urological procedures (such as cystoscopy, bladder biopsy, or the placement of urological implants), contributing to a lower use of antibiotics and a decrease in iatrogenic bacterial UTIs. Urinary catheters should be reserved for strictly necessary cases and for the shortest possible time. A significant percentage of catheterized dogs and cats (10 to 50%) develop bacterial UTIs. The risk increases with the catheterization time and in the presence of urinary injuries (Bartges, 2012; Bubenik et al., 2007; Bartges, 2012; Weese et al., 2019). In fact, Sullivan et al. (2010) found that the probability of infection increases by 27% for every additional day of catheterization. The use of an anti-sepsis protocol to fix and maintain the catheter has helped to reduce the frequency of bacteriuria. Weese et al., (2019) recommended using closed collection systems and discouraged the use of prophylactic antibiotics in catheterized animals. Urine cultures, as well as empirical treatment, in the absence of clinical signs of UTI, should be avoided; and catheter cultures are not predictive of UTI development (Weese et al., 2011; Weese et al., 2019).

Conclusions

The clinical and epidemiological aspects presented in this review provide valuable insights into the prevalence, diagnosis, and management of UT infections (UTIs) in dogs and cats. UTIs are relatively common in companion animals, with females being more susceptible, and can be associated with various predisposing factors such as underlying health conditions and anatomical differences. The diagnosis of UTIs typically involves urinalysis and culture to identify the causative microorganisms. *Escherichia coli* is a common pathogen, but other significant bacterial possibilities exist. Antimicrobial prescription is a common practice for UTI treatment, but the growing concern of antimicrobial resistance necessitates a cautious approach to antibiotic stewardship. Understanding UTIs in companion animals is essential for informing veterinary practices and guiding antibiotic stewardship efforts.

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Bakterijske infekcije urinarnog trakta u veterinarskim ordinacijama za male životinje – klinički i epidemiološki aspekti

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Infekcija urinarnog trakta (UTI) uobičajena je bolest u pasa i mačaka i može se pojaviti kao izolirana ili ponavljana infekcija. Slučajevi ponavljane infekcije posebno su uobičajeni u slučajeva s pozadinskim zdravstvenim problemima. Dijagnoza UTI u pasa i mačaka općenito podrazumijeva integriranu interpretaciju kliničkih znakova, analizu mokraće i bakterijske kulture. Dijagnostičko oslikavanje tmože pomoći i procijeniti ili odbaciti anatomske lezije. Jedan od brojnih mikroorganizama koji mogu prouzročiti UTI jest Escherichia coli. Ženke, gerijatrijski pacijenti i životinje s komorbiditetima obično imaju povećani rizik od UTI. Antimikrobni lijekovi su uobičajeni za liječenje UTI u kućnih ljubimaca. Danas postoji sve veća zabrinutost zbog antimikrobne rezistencije zbog prekomjerne uporabe antibiotika koja dovodi do odabira za rezistenciju. Stoga su ispravni lijek i odgovarajuće vođenje pacijenta od osnovne važnosti. Ovaj pregled ima za cilj dati sažetak kliničkih i epidemioloških aspekata UTI, doprinoseći poboljšanju veterinarskih praksi i propisivanju antibiotika u kontekstu UTI u kućnih ljubimaca.

Ključne riječi: *mačke, klinički znaci, psi, epidemiologija, infekcije urinarnog trakta*