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URINARY TRACT INFECTIONS OF SMALL ANIMALS: LITERATURE REVIEW

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Abstract: Urinary tract infections are quite common in the clinical routine of small animals and have become one of the main causes of antimicrobial prescriptions. Treatment based solely on the presence of clinical signs, without performing a urine culture, can lead to errors and contribute to the increase in bacterial resistance to antimicrobials. A complete and targeted anamnesis, the recognition of specific clinical signs and the performance of complementary exams enable the diagnosis of cystitis, which can be either bacterial or simply inflammatory. The most common complementary tests to be performed are urinalysis and abdominal ultrasound. The gold standard for confirming the presence of bacteria and their susceptibility is bacterial urine culture and antimicrobial susceptibility testing (AST). This literature review aims to cover the most common small animal urinary tract infections in the veterinarian's routine and their appropriate treatments. The references selected for the review were obtained from the following international databases: PubMed, SciELO and Google Scholar.
Keywords: urinary tract infection; little animals; urine culture; urinalysis

INTRODUCTION

Urinary tract infections (UTI) are quite common in the clinical routine of small animals (Bloch et al., 2022). It consists of the presence of an infectious agent, which adheres and multiplies in the urinary system, generating an inflammatory response and the appearance of clinical signs, consequently becoming one of the main causes of antimicrobial prescription in clinical routine (Dorsch et al., 2019; Weese et al., 2019).

With concerns surrounding the increase in antimicrobial resistance, and the rampant use of antibiotics in the treatment of UTIs without prior culture (Dorsch et al., 2019), a guideline was published to assist veterinarians in the correct diagnosis and treatment of UTIs in dogs and cats (Weese et al., 2019).

Bacterial cystitis traditionally classified as complicated and uncomplicated (Weese et al., 2011) is now classified into sporadic bacterial cystitis, recurrent bacterial cystitis and subclinical bacteriuria (Weese et al., 2019).

The beginning of a good diagnosis of bacterial cystitis is done with the help of a complete and targeted anamnesis, carried out by a professional capable of evaluating and recognizing clinical signs and requesting complementary tests (Barsanti, 2015; Weese et al., 2019).

REVIEW OF LITERATURE

ANATOMY OF THE URINARY TRACT

The urinary tract is made up of the kidneys, ureters, urinary bladder, urethra and female or male genitals (König et al., 2009; Smith, 2010). The organs that make up this system produce, transport, store and eliminate urine in a coordinated manner (Fowler et al., 2008; Hickling et al., 2016). This process allows the elimination of metabolites and toxic products from the body, in addition to playing a fundamental role in eliminating possible microorganisms invading the urinary tract (Hickling et al., 2016).

The urinary bladder is a hollow organ whose shape, size and position vary according to its distension depending on the amount of urine stored, located on the pubic bones and stretching cranially towards the abdomen (König et al., 2009; Smith, 2010). Its wall is mainly composed of smooth muscle and collagen (Hickling et al., 2016). The urinary bladder is surrounded by a double layer of peritoneum and is divided into three portions: cranial apex, intermediate body and caudal neck, the latter of which funnels to the cranial portion of the urethra (König et al., 2009). The female urethra is short, straight and wide, while the male urethra is long, curved and narrow; both empty into the external ostium of the urethra, which is surrounded by skeletal muscles and provides voluntary control of urination (Smith, 2010).

When not eliminating urine, the urinary tract is efficient at remaining a closed system in order to become inaccessible to microorganisms (Hickling et al., 2016).

URINARY TRACT INFECTIONS

UTIs consist of the adherence, multiplication and persistence of an infectious agent in the urinary system associated with the presence of an inflammatory response and clinical signs (Dorsch et al., 2019). UTIs are quite common in the veterinary clinical routine of small animals, being more prevalent in dogs (Bloch et al., 2022). It is estimated that 14% of dogs will develop bacterial cystitis at some point in their lives (Ling, 1984). In a retrospective study conducted by Hall et al. (2013), 14.8% of dogs treated over a ten-year period had a positive urine culture. In cats, the prevalence of UTI is less than 3% (Byron, 2018), and may be more frequent in felines with comorbidities, such as chronic kidney disease, hyperthyroidism and diabetes mellitus (White et al., 2013), reaching 40-45 % in felines over 10 years of age (Dorsch et al., 2019).

Several factors have already been associated with the development of UTIs in both species, such as sex, age, comorbidities and functional abnormalities of the lower urinary tract (Byron, 2018). Regarding sex, females are more affected by bacterial cystitis in both species (White et al., 2016; Puchot et al., 2017; Yu et al., 2019; Scarborough et al., 2020). This is due to the proximity of the rectum and vulva and the anatomical differences of the female urethra, making them more susceptible to infection by ancestry, given that the primary source of bacteria invading the lower urinary tract are the colon and skin (Byron, 2018; Lamoureux et al., 2019; Stępień-Pyśniak et al., 2021). In males (canines or felines or both??), the presence of prostatic secretions containing zinc, a bacteriostatic substance, and the anatomy of the urethra, long and tortuous, are protective factors and make them less susceptible to the development of UTI (Smee et al, 2013; Lamoureux et al., 2019).

Regarding breed, although no predisposition has been established in dogs to date (Thompson, 2011; Yu et al., 2019), a study observed a higher prevalence in large and giant breeds among younger patients diagnosed with UTI (Ling et al., 2001). In cats, the Abyssinian (Lekcharoensuk et al., 2001) and Persian (Dorsch et al., 2014) breeds seemed to be most affected.

UTI is one of the main causes of the prescription of antimicrobials in clinical routine, and poorly executed treatment can represent a series of problems, both for the patient, due to the failure to resolve the problem, and for public health due to the development of resistance to antimicrobials (Weese et al., 2019).

Complementary tests, such as blood count, biochemistry, urinalysis and abdominal ultrasound, are important for the diagnosis of cystitis and, in addition, provide information about the patient's general condition and severity of the UTI (Smee et al., 2013; Lamoureux et al., 2019).

The majority of UTIs are caused by bacterial agents, with less than 1% caused by fungal, parasitic and viral agents (Dorsch et al., 2019). Escherichia coli is the bacteria most frequently isolated in cases of UTI in dogs and cats (Puchot et al., 2017; Byron, 2018; Punia et al., 2018; Dorsch et al., 2019), followed by Staphylococcus spp., Enterococcus spp., Proteus spp. and Klebsiella spp. in dogs (Byron, 2018; Punia et al., 2018; Scarborough et al., 2020) and by Streptococcus spp., Enterococcus faecalis and Staphylococcus felis in cats (Puchot et al., 2017; Dorsch et al., 2019).

BACTERIAL CYSTITIS AND ITS CLASSIFICATION

Sporadic bacterial cystitis is a common condition in dogs and less frequent in cats (Bloch et al., 2022), often referred to as uncomplicated UTI (Weese et al., 2019), in which bacterial infection of the urinary bladder results in inflammation (Dorsch et al., 2019). Sporadic bacterial cystitis is an infection that occurs in non-pregnant females or healthy castrated males, in animals without any anatomical or functional abnormality of the urinary tract or any relevant comorbidity, and in animals that have had less than three episodes of bacterial cystitis in twelve previous months. However, an animal with urinary tract abnormalities or comorbidities does not always have a substantially higher risk of complications or recurrent infections, but may instead develop sporadic bacterial cystitis. This type of cystitis appears to be less common in unneutered male dogs, and bacterial prostatitis must be considered in these animals with lower urinary tract signs (Wood, 2016; Weese et al., 2019).

Recurrent bacterial cystitis is characterized by the occurrence of three or more episodes of bacterial cystitis in the preceding twelve months or two or more episodes in the preceding 6 months (Weese et al., 2019; Dorsch et al., 2019). This type of cystitis can occur due to recurrence of infection, persistence of infection or reinfection (Wood, 2016; Weese et al., 2019). Recurrent cystitis is considered to be one that occurs due to the same microorganism after successful treatment of the initial cystitis (Dorsch et al., 2019). In this case, the urine becomes sterile after treatment, but reservoirs of bacteria allow the urine to recolonize within a few days or weeks (Wood, 2016). Persistent cystitis is considered to be one that has persistent positive urine cultures showing the same microorganism even after adequate treatment has been carried out, using appropriate drug, dosage and duration (Wood, 2016; Dorsch et al., 2019). This possibly occurs due to one or more of the following three factors: development of antimicrobial resistance by the bacteria, impairment of the host's immune system and/or because the minimum inhibitory concentration of antibiotic in the urine that would be capable of preventing bacterial isolation has not been reached (Wood, 2016). Reinfection is considered to be cystitis that occurs due to a microorganism different from the initial cystitis after responding to therapy (Weese et al., 2019; Dorsch et al., 2019). In this case, it is important to look for possible factors that predispose this patient to UTI (Wood, 2016; Weese et al., 2019). In both recurrent cystitis and reinfection, the urine becomes sterile for a period, making it difficult to differentiate between them, however, it is important to do so, as the therapeutic approach of one differs from the other (Wood, 2016).

It is common to compare the antimicrobial susceptibility patterns of one infection and another, but this is not a reliable method, as these patterns can change even in the same microorganism (Drazenovich et al., 2004; Freitag et al., 2006). The definitive method for differentiating recurrent cystitis from reinfection is by pulsed-field electrophoresis genotyping (Drazenovich et al., 2004; Wood, 2016).

It is worth noting that a single recurrence of sporadic bacterial cystitis, when it occurred within the preceding three months, must be treated as recurrent bacterial cystitis (Weese et al., 2019).

Subclinical bacteriuria occurs when there is a positive urine culture of urine properly collected in a sterile manner, with the absence of clinical signs that indicate UTI (Dorsch et al., 2019), therefore, the observation of bacteria only with cytological analysis of urine is not considered subclinical bacteriuria. (Weese et al., 2019). It is important to remember that, as previously described, UTI is defined not only by the presence of bacteria in the urine, but by its adherence, proliferation and persistence associated with clinical signs of the lower urinary tract, such as urinary frequency, hematuria, dysuria and/or strangury (Byron, 2018; Weese et al., 2019; Dorsch et al., 2019). Therefore, the presence of bacteria in urine is not a diagnosis of UTI (Wood, 2016). The most frequent pathogens found in subclinical bacteriuria are Escherichia coli and Enterococcus faecalis (Litster et al., 2009; Wan et al., 2014).

Subclinical bacteriuria is not an uncommon finding in dogs, even in individuals without predisposing factors (Weese et al., 2019), reaching 12% in healthy dogs (O'Neil et al., 2013; Wan et al., 2014) and from 15 to 74% in dogs with comorbidities (Weese et al., 2019). In cats, the prevalence of subclinical bacteriuria varies from 0.9 (Eggertsdóttir et al., 2011) to 29% (Litster et al., 2009), with no significant difference noted in animals with comorbidities (Moberg et al., 2019), however, females appear to be more affected (Eggertsdóttir et al., 2011; Litster et al., 2009; Dorsch et al., 2019).

CONCOMITANT DISEASES AND/OR COMORBIDITIES

Several concomitant illnesses and comorbidities have already been considered predisposing factors for UTI and positive urine cultures in both canine and feline species (Weese et al., 2019). Among endocrinopathies, diabetes mellitus is repeatedly mentioned (Forrester et al., 1999; Mcguire et al., 2002; Mayer-Roenne et al., 2007). The greater predisposition to the development of UTI in diabetic patients is due to a series of factors, such as impaired neutrophil function, abnormal cellular immunity and lower antibacterial activity of urine due to dilution and the presence of glucose (Bailiff et al., 2006). A prevalence of 12% to 37% of UTI in diabetic patients has been reported (Forrester et al., 1999; Mayer-Roenne et al., 2007). In these patients, there is also a greater risk of developing pyelonephritis (Mayer-Roenne et al., 2007) and emphysematous cystitis due to the large amount of glucose in the urine, favoring bacterial fermentation (Dorsch et al., 2019).

Hyperthyroidism in felines is also cited as an endocrinopathy predisposing to UTIs, with a prevalence of 12% (Mayer-Roenne et al., 2007; Dorsch et al., 2019). In dogs, UTIs were common in patients with hyperadrenocorticism, present in 46% of cases (Forrester et al., 1999). It is suggested that this predisposition is due to urine dilution, glycosuria that affects neutrophil chemotaxis, and suppression of the immune system due to hypercortisolemia (Ihrke et al., 1985).

Obesity can predispose to UTI due to several factors (Wynn et al., 2016), such as restricted mobility, as obese individuals are more likely to develop osteoarthritis, reducing the frequency of urination (Marshall et al., 2009), in addition to greater propensity to develop skin and perineal infections that can ascend to the urinary tract (Wynn et al., 2016).

Chronic kidney disease is also frequently associated with UTIs (Mayer-Roenne et al., 2007; White et al., 2013; Puchot et al., 2017; Foster et al., 2018; Lamoureux et al., 2019), reporting there is a prevalence of 22 and 29% in cats with chronic kidney disease (Mayer-Roenne et al., 2007; White et al., 2013). It is also worth noting that around a third of these feline patients may present a positive urine culture (Dorsch et al., 2019) and 18.1% of canine patients with chronic kidney disease presented bacteriuria in one study (Foster et al., 2018).

Immunosuppressive therapies have an effect on the development of UTIs. Dogs on long-term treatment with corticosteroids have a chance of developing UTI more frequently (Ihrke et al., 1985; Peterson et al., 2012).

Congenital urogenital anomalies can also facilitate the development of UTI (Weese et al., 2019), for example, ectopic ureters lack a functional vesiculoreteral valve, allowing the ascendance of the infection (Smee et al., 2013), as well as other anatomical defects and/or or acquired conditions, such as urethral rupture, urethrostomy (Lekcharoensuk et al., 2001; Thompson, 2011; Weese et al., 2019), urolithiasis (Thompson, 2011; Wynn et al., 2016; Weese et al., 2019), tumors or urinary bladder neoplasia (White et al., 2016; Dorsch et al., 2019; Weese et al., 2019) and prostate disease (Thompson, 2011; Smee et al., 2013; Byron, 2018; Dorsch et al., 2019). In dogs, unlike cats, struvite uroliths are almost always induced by infection; in cats, most uroliths are sterile (Weese et al., 2019).

Incontinence or urinary retention is also a predisposing factor to the development of UTI (Olby et al., 2016; Byron, 2018; Weese et al., 2019; Dorsch et al., 2019) and can be found in 4% of UTI cases. diseases of the lower urinary tract of felines, being more common in the Manx breed (Lekcharoensuk et al., 2001), and can also affect animals that have suffered a thoracolumbar injury (Olby et al., 2016).

Polypoid cystitis is a rare form of complicated UTI (Dorsch et al., 2019), consisting of the proliferation of masses or thickenings in the urinary bladder mucosa induced by inflammation, most commonly associated with Proteus spp. infections. (Martinez et al., 2003), which may resolve with antimicrobial therapy alone or may require surgical intervention (Wolfe et al., 2010).

Other conditions previously related to UTI were: gastrointestinal infections, due to fecal contamination of the genitalia (Koutinas et al., 1998; Dorsch et al., 2019), spinal cord injury, due to limited mobility and incontinence or urinary retention (Olby et al., 2016; Baigi et al., 2017) and, in cats, liver disease, although the reason for this is not completely elucidated, cirrhotic humans are more prone to bacteriuria and UTI (Moberg et al., 2019).

DIAGNOSIS OF BACTERIAL CYSTITIS

The diagnosis of bacterial cystitis can be aided by the presence of some clinical signs such as urinary frequency, stranguria and hematuria (Byron, 2018; Dorsch et al., 2019; Weese et al., 2019). Despite aiding in diagnosis, these clinical signs are nonspecific and can be seen in other diseases of the lower urinary tract, such as feline idiopathic cystitis (FIC) (Dorsch et al., 2019). Systemic signs, such as fever, will rarely be found (Barsanti, 2015; Byron, 2018), unless the animal has a concomitant disease, such as prostatitis and pyelonephritis. Animals may experience discomfort when palpating the urinary bladder, around the kidneys and prostate if they have pyelonephritis or prostatitis associated with UTI. There may be excessive cleaning of the genitals by dogs and cats, contributing to irritation of the penis or vulva (Byron, 2018).

Although the presence of clinical signs is extremely important for diagnosis, it is important to highlight that bacterial cystitis can also present asymptomatically (Barsanti, 2015; Byron, 2018; Weese et al., 2019), with the symptomatic form being related the quantity of causal organisms, virulence factors that will determine not only the severity of the disease but also the location of the infection, the presence of predisposing causes and also the immunological response of the individual's body to the infection (Dorsch et al., 2019). In felines, for example, the healthy urinary tract is a hostile environment for bacterial migration and colonization. They perform frequent and complete emptying of the bladder, there is the presence of normal resident microflora and the anatomy of the urinary tract is favorable (Dorsch et al., 2019). Although bacterial cystitis is a common infection in dogs, and little observed in cats, since idiopathic cystitis is more common in felines (Dorsch et al., 2019), attempting a diagnosis based exclusively on clinical signs can lead to errors being It is essential to carry out additional tests, such as urinalysis (Barsanti, 2015).

Urinalysis is a simple and relatively low-cost test that provides important information about urinary tract disorders and is of great support for the diagnosis of bacterial cystitis. Despite this, this examination may suffer external interference (Reppas & Foster, 2016). Normally, bacteria can be present in the urethra, vagina and foreskin, so the identification of bacteria in urine is not synonymous with UTI. Urine samples obtained by spontaneous urination or urethral catheter may suffer from external contamination, which is why cystocentesis is the preferred method for collecting material from patients with suspected UTI, providing contaminant-free samples (Byron, 2018; Dorsch et al., 2019). The urine sample must also be obtained before starting antimicrobial treatment and following storage recommendations, an important factor that can influence test results due to altered pH, lysis of casts, leukocytes and epithelial cells, precipitation of substances and formation of in vitro crystals. Inadequate storage can also lead to bacterial contamination and proliferation as well as bacterial death. (Dorsch et al., 2019).

The urinalysis examination includes macroscopic and microscopic evaluation, in which the macroscopic examination allows the evaluation of the appearance of the urine in general (physical examination), while the microscopic evaluation consists of examination of urinary sediments with cytological evaluation (Reppas & Foster, 2016). The chemical urine test relies on the analysis of reagent strips, which can often reveal hematuria and proteinuria in cases of bacterial cystitis (Dorsch et al., 2019). It is important to note that the strips used in the chemical assessment of urine are less accurate in detecting UTIs in small animals than in humans (Byron, 2018).

Assessment of urinary sediment is an important step towards diagnosing bacterial cystitis (Dorsch et al., 2019). It may present findings indicative of UTI, namely: bacteriuria, pyuria and hematuria, the first being the most specific. Leukocytes may also be observed, which are indicative of inflammatory lesions of the urinary tract (Barsanti, 2015). However, some sediment findings in cats with bacterial cystitis may be present in other conditions, such as hematuria, which is also present in more than 70% of cats with feline idiopathic cystitis, and in the majority of cats with urolithiasis and feline neoplasia. urinary bladder. Pyuria is also a reported finding in up to 77% of cats with feline idiopathic cystitis and more than 50% of cats with urocystolith (Dorsch et al., 2019).

In addition to changes in urinalysis, animals with bacterial cystitis may or may not present hematological changes. Normally, in most animals without concomitant diseases, no relevant changes in blood counts are observed (Smee et al., 2013). Regarding the assessment of serum biochemistry, most of the time no changes are observed, except where there are complications or concomitant diseases present (Bailiff et al., 2008; Smee et al., 2013; Barsanti, 2015), e.g. in pyelonephritis, kidney disease and prostate disease, in which elevations in renal markers, such as creatinine, urea and symmetric dimethylarginine (SDMA) may be observed (Weese et al., 2019).

Diagnostic imaging tests, such as ultrasound, can be a complementary means of diagnosing bacterial cystitis (Dorsch et al., 2019; Weese et al., 2019), especially in cases of recurrent cystitis (Weese et al., 2019), aiming to identify the presence of regular or irregular thickening of the bladder wall and evaluate possible concomitant changes (Barsanti, 2015; Weese et al., 2019).

Urine culture is considered essential in the definitive diagnosis of bacterial cystitis (Byron, 2018; Dorsch et al., 2019; Weese et al., 2019). As with urinalysis, it is important to pay attention to the technique for obtaining the sample, always prioritizing cystocentesis (Dorsch et al., 2019; Weese et al., 2019). Additionally, storage at room temperature leads to a rapid increase in the number of bacteria, so urine samples must be refrigerated as quickly as possible and processed in a microbiology laboratory within 24 hours. Most uropathogens are cultured over an 18 to 24-hour incubation period. However, there are some slow-isolating pathogens, such as Corynebacterium species, that may require a longer time to appear on plaques. Furthermore, it is important to remember that most bacterial cystitis is caused by a single bacterial pathogen (Dorsch et al., 2019). Escherichia coli is the most isolated pathogen in feline urine, with Streptococcus, Enterococcus and Staphylococcus species also frequently documented (Dorsch et al., 2019). The bacteria commonly isolated in the urine of dogs with bacterial cystitis are the gram-negative ones, Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Proteus mirabilis and Enterobacter spp., and the gram-positive Streptococcus spp. and Staphylococcus spp. (Barsanti, 2015; Yu et al., 2019).

TREATMENT OF BACTERIAL CYSTITIS

Bacterial cystitis is among the most important reasons for the use of antimicrobials in veterinary medicine, and consequently contributes to the development of antimicrobial resistance. Antibiotics of great pharmacological importance, such as cephalosporins and fluoroquinolones, are frequently used to treat cats with bacterial cystitis without prior culture (Dorsch et al., 2019). Antimicrobial therapy must be based on the presence of clinical signs, the presence or absence of concomitant diseases, and the results of urine culture and TSA (Dorsch et al., 2019; Weese et al., 2019). Some animals with bacterial cystitis may require treatment before definitive TSA results are obtained (Dorsch et al., 2019). It is important to emphasize that treatment prior to the TSA result is rarely indicated, as it contributes to an increase in bacterial resistance, repeated infections and complications associated with the indiscriminate use of antimicrobials (Weese et al., 2019). When recommended, empirical treatment must be based on site-specific bacterial prevalence rates and antimicrobial resistance patterns (Dorsch et al., 2019; Weese et al., 2019). In general, amoxicillin is often a reasonable first choice in most areas, and there is no evidence for the need for association with clavulanic acid. The use of Sulfamethazole/Trimethoprim is another first-line option, but it has greater adverse effects (Weese et al., 2019).

In general, in cases of uncomplicated (sporadic) cystitis, to relieve pain, analgesics can be administered while awaiting culture results. If treatment is necessary prior to culture and TSA results, amoxicillin or Sulfamethazole/Trimethoprim are indicated for shorter treatment periods (3-5 days) (Dorsch et al., 2019; Weese et al., 2019). If there is no clinical improvement and the chosen antimicrobial is insufficient based on the original TSA, it must be discontinued and an investigation into the reason for failure must begin (Byron, 2018; Dorsch et al., 2019). Nitrofurantoin, fluoroquinolones and 3rd generation cephalosporins are antibiotics that must be reserved in cases of sporadic cystitis unresponsive to amoxicillin and Sulfamethazole/Trimethoprim, based on culture results and sensitivity tests, or even in cases of individual patient factors (Weese et al., 2019).

In cases of recurrent cystitis, depending on the severity of clinical signs, treatment with analgesics alone may be considered while awaiting urine culture results. However, in certain cases, as well as in sporadic cystitis, empirical therapy may be established (Weese et al.,2019). A treatment period of 3 to 5 days must be considered in cases of reinfection, while 7 to 14 days may be indicated in the treatment of persistent or potentially recurrent infections (Dorsch et al., 2019; Weese et al., 2019).

BACTERIAL RESISTANCE AND MULTIDRUG RESISTANCE

In veterinary medicine there are a relatively large number of antimicrobial agents that can be used for clinical purposes in the treatment of bacterial cystitis (Scarborough et al., 2020). However, antimicrobial susceptibility testing (ASR) is necessary to prevent or reduce the incidence of antimicrobial resistance (Yu et al., 2019; Scarborough et al., 2020). In some regions, such as northern Europe, there is a lower prevalence of bacterial resistance or multiresistance, which can be explained by the more restrictive use of antimicrobials in these regions, highlighting the importance of targeted antibiotic therapy (Dorsch et al., 2019).

Rates of resistance to antimicrobials used in companion animals have increased over the years (Dorsch et al., 2019). This isolation can be justified by the large-scale use of broad-spectrum antibiotics without carrying out complementary tests and prior TSA (Ishii et al., 2009).

Currently, there is an increasing prevalence of resistance to antimicrobials isolated from the urinary tract, particularly in the class of fluoroquinolones, cephalosporins and β-lactams + clavulanic acid (Cohn et al., 2003; Gibson et al., 2008; Thompson, 2011), which are antimicrobial agents effective against gram-negative pathogens and available in oral formulations, being widely used (Thompson, 2011).

Bacteria have remarkable genetic plasticity and are capable of responding to various environmental threats, including the presence of antimicrobials (Munita & Arias, 2016). Antimicrobial resistance mechanisms in bacteria can be intrinsic or acquired. Intrinsic mechanisms are those referring to the characteristics of the microorganism that make it intrinsically resistant to a class of antimicrobials (Mulvey & Simor, 2009), such as the resistance of anaerobic bacteria to aminoglycosides (Krause et al., 2016), which occurs due to the need for aerobic metabolism for the mechanism of action of this antimicrobial (Legget, 2016).

Acquired mechanisms are those in which a genetic change occurs in the microorganism, either through mutation or through the acquisition of new genetic information (Mulvey & Simor, 2009). Mutation is an uncommon event, occurring in one in every one million to one billion cell divisions, and the majority of these mutations are harmful to the cell (Mulvey & Simor, 2009; Reygaert, 2018). Mutations that confer resistance are those that occur in specific genes, such as those that encode the drug target (Reygaert, 2018).

The acquisition of genetic material can occur through transformation, transduction and conjugation (Munita & Arias, 2016; Reygaert, 2018). Transformation is the incorporation by bacteria of genetic material present in the environment; transduction is the incorporation of genetic material accidentally transported from one bacterium to another; and conjugation, which is the most important form of them, occurs sexually, through the exchange of genetic material between two bacteria, (Munita & Arias, 2016).

Biochemically, bacteria can become resistant through some mechanisms: 1) modification/inactivation of the antibiotic molecule through enzymatic action, 2) reduced permeability or increased efflux of antimicrobials, 3) change in the drug's site of action and 4) changes in the cell as a whole (Munita & Arias, 2016).

In addition to the large-scale use of antibiotics, other factors justify bacterial resistance (Mulvey et al., 2000). Resistance to antibiotic treatment of diseases of the urinary system may be related to the ability of bladder epithelial cells to endocytosis bacteria through the defense mechanism, providing an environment rich in nutrients (Lewis et al., 2016). This is favorable to its replication or persistence, as with bacterial expression of type 1 fimbriae, apoptosis and exfoliation of the bladder mucosa can occur (Mulvey et al., 2000).

Another mechanism related to bacterial resistance is the formation of bacterial biofilms, causing changes in the metabolism of bacteria and consequently better cell-to-cell communication, in addition to increasing their ability to evade the host's immune response and the effects of antimicrobials through metabolism. isolated along with physical and chemical protection of the biofilm matrix (Talagrand-Reboul et al., 2017; Singh et al., 2017). Acquired resistance of bacteria to antibiotics can also develop through sporadic mutations in intrinsic genes or through horizontal gene transfer (Dorsch et al., 2019).

The classification suggested by Magiorakos and collaborators in 2012 is the classification adopted by the National Health Surveillance Agency (ANVISA) and cited in the manual "Prevention of infections by multi-resistant microorganisms in health services" (2021), and determines that for the bacteria to be considered multidrug-resistant (MDR), it must be resistant to three or more categories of antimicrobials tested. The same author also suggests a classification for what he calls extensively drug-resistant (XDR) bacteria, which encompasses bacteria resistant to all but two or fewer categories of tested antimicrobials; and all drug resistant (PDR) bacteria, comprising bacteria resistant to all categories of antimicrobials tested (Magiorakos et al., 2012).

FINAL CONSIDERATIONS

Given that urinary tract infections in small animals are quite common in clinical routine and are therefore one of the main causes of prescription of antimicrobials in clinical routine, it is important that the veterinarian knows how to identify the clinical signs and concomitant diseases that may occur, direct the request for complementary tests and carry out treatment effectively, in order to avoid the increase in antimicrobial resistance with the rampant use of antibiotics.

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