

## Summary

Urinary tract disorders pose significant challenges to the health of companion carnivores, impacting their quality of life and requiring prompt and efficient management. Comprehensive urine analysis, often referred to as "liquid gold" due to the valuable insights it provides, plays a crucial role in understanding and managing lower urinary tract conditions.

The research underlying the doctoral thesis titled "Research on etiopathogenesis, diagnosis, and treatment of urinary bladder disorders in pet carnivores" was conducted between October 2019 and February 2024, both at the veterinary medical clinic S.C. SANIVET S.R.L. in Iași and at the Faculty of Veterinary Medicine in Iași. The thesis aimed to enhance current diagnostic and treatment options for these conditions. Through a systematic exploration of etiological factors, diagnostic modalities, and therapeutic interventions, this study sheds light on the complexity of urinary bladder disorders in companion carnivores and offers valuable insights for veterinary practice.

The thesis comprises 176 pages and is structured into two parts. The first part includes a literature review on the topic, spanning 42 pages, while the second part presents personal research findings, totaling 83 pages. Additionally, the thesis includes a table of contents, list of abbreviations, introduction, abstract, bibliography, and annexes. This work features 73 figures and 25 tables, drawing upon 173 bibliographic sources.

**The first chapter**, entitled "*Ontogenesis and Histology of the Urinary Tract*," is structured into two sub-chapters. The first sub-chapter discusses the formation of the urinary apparatus during the embryonic period, describing the formation of the pronephros, mesonephros, and metanephros, as well as the definitive structures that arise from them. The second sub-chapter describes the histological structures of the kidneys and urinary pathways.

**The second chapter**, "*Anatomy and Physiology of the Urinary Tract*," is structured into two sub-chapters. The first sub-chapter covers the anatomical elements of the urinary apparatus, while the second sub-chapter covers aspects of kidney and urinary pathway physiology.

**In the third chapter**, titled "*Etiopathogenesis of Urinary Bladder Disorders in Companion Carnivores*", the etiological factors and mechanisms underlying the development and progression of urinary pathologies commonly encountered in veterinary practice are detailed.

The second part, "Personal Research," spans five chapters, presenting and discussing the results of the research conducted throughout the study.

**Chapter 4**, titled "*Aims and Objectives of the Research*", addresses the motivation behind the choice of research topic, driven by limited information on bladder pathologies in companion carnivores from northeastern Romania. The aim of the doctoral thesis was to augment current diagnostic and treatment options for these conditions. To achieve this, several general objectives were pursued, including an extensive review of specialized literature, the initiation of judicious treatment, and the identification of solutions to optimize diagnostic and treatment methods for urinary bladder conditions.

The research was conducted in relation to several specific objectives.

**Chapter 5**, entitled "*Clinical and Paraclinical Investigations*", comprises two sub-chapters presenting the results of clinical and paraclinical investigations. A total of 161 patients were consulted during the study, with uropathies recorded in 5.54% of all examined patients. Remarkably, the incidence of lower urinary tract disorders was higher in cats (4.1%, 119 cases) compared to dogs (1.44%, 42 cases), with feline idiopathic cystitis and obstructive uropathy being the most frequent pathologies encountered in cats,

while infectious cystitis predominated in dogs. Various factors such as age, sex, reproductive status, and body mass were found to influence the risk of urinary pathologies.

In the sub-chapter entitled "*Imaging Examination in Patients with Uropathies*", the imaging aspects encountered in various urological pathologies are presented. Ultrasound was most commonly used, being an essential tool in identifying urinary bladder anomalies. Ultrasound examination was available for 84 feline patients out of 119 and for all 42 canine patients examined clinically. In cats, the most frequent anomaly associated with the urinary bladder was the presence of sediment (66 out of 84 cats examined sonographically, 78.57%). Forty male cats were sonographically examined after cessation of urination for a duration ranging from 24 to 72 hours, showing changes directly proportional to the duration and severity of the obstruction. The most significant changes, associated with renal function impairment, were urethral dilatation, pyelectasis, and the presence of perivesical fluid. These changes were correlated with the presence of severe hyperkalemia. Ultrasound also proved its utility in identifying comorbidities that may coexist with cystitis, such as pyometra or prostatic diseases. Additionally, with a high positive predictive value in stone detection, color Doppler ultrasound allowed the association of mosaic appearance with stone presence. Radiological examination was used both before and after cystotomy to assess the presence of stones.

In the sub-chapter entitled "*Urinary Examination in Patients with Uropathies*", the results of examining a total of 109 urine samples were discussed. In dogs, urinary sediment revealed the predominance of formed elements from the blood circulation (pus - 15 samples/57.69%; hematuria - 12 samples/46.15%), followed by microorganisms (7 samples/26.92%). In cats, urinary sediment predominantly revealed struvite crystals (63 out of 83 analyzed samples - 75.9%). Microscopic examination of the urinary sediment provided information about the aggregation behavior of the crystals, which was correlated with urinary pH. Additionally, microscopic examination allowed the observation of the predominance of rough aspects on certain crystal faces, favoring bacterial adhesion. Moreover, microscopic examination allowed the identification of yeasts and parasitic elements.

**Chapter 6, "*Results of Bacteriological Investigations*"**, covers the microbial profiles and antibiotic resistance observed in urinary tract infections in companion carnivores. The investigations were conducted on 102 urine samples collected from 64 cats and 38 dogs diagnosed with infectious uropathy. Urine collection was performed by catheterization or cystocentesis. In the current study, a higher degree of resistance was encountered in Gram-negative bacteria compared to Gram-positive ones. Among Gram-negative bacteria, *Escherichia coli* was most frequently isolated, while *Enterococcus faecalis* was the most common Gram-positive bacterium in both dogs and cats. Twelve antibiotics were tested, classified into eight different classes: aminopenicillins + beta-lactamase inhibitors, aminoglycosides, amphenicols, fluoroquinolones, sulfonamides, lincosamides, tetracyclines, and cephalosporins. In cats, Gram-positive bacteria exhibited high resistance to chloramphenicol. No resistances were observed against florfenicol, marbofloxacin, lincomycin, doxycycline, and oxytetracycline. In contrast, Gram-negative bacteria showed extensive resistance to several antibiotics, especially to enrofloxacin (34.21%). In dogs, a higher resistance rate was encountered for florfenicol (27.27%), while the most susceptible antibiotic was oxytetracycline (81.81%).

In both animal species, Gram-negative bacteria exhibited reduced sensitivity to the tested antibiotics. Marbofloxacin was the most effective antibiotic in 60% of cases in dogs and in 52.63% of cases in cats. Surprisingly, a 50% resistance of Gram-positive bacteria to chloramphenicol was noted in cats, although there was no recorded abuse in the use of these antibiotics. The interpretation of the results allowed the delineation of a local profile of antibiotic sensitivity and resistance. Significant variations in antibiotic

resistance reported in previous studies indicate the need for regular monitoring of bacterial sensitivity through urine cultures and antibiograms.

**Chapter 7**, "*Therapy of Urinary Bladder Conditions*", outlines the multimodal therapy performed for each category of condition encountered during the study. A notable aspect highlighted in this study is the importance of medicinal dissolution of struvite calculi. An 8.2 mm calculus, detected sonographically in a 2-year-old sterilized cat weighing 3.4 kg, was completely dissolved in 206 days (6 months and 23 days). The progress of dissolution was closely monitored through periodic clinical and sonographic examinations, emphasizing the effectiveness and feasibility of this therapeutic approach. Active involvement and cooperation of the owners proved to be essential in ensuring the success of therapeutic interventions and the overall well-being of the non-verbal patients.

In conclusion, the conducted research provides valuable insights into various aspects of urinary bladder pathologies in companion carnivores. Following comprehensive urine analysis and clinical investigations, several key findings have been highlighted. The identification of calcium oxalate in numbers greater than five crystals per microscopic field at 400x magnification, crystals with distinct morphology and behaviors, yeast, or *Capillaria plica* eggs, underscores the importance of microscopic examination of all biological samples for accurate diagnosis.

Remarkably, statistical analysis has revealed a correlation between overweight/obesity and the occurrence of uropathies, with 51.5% of diagnosed patients falling into the overweight or obese category. Within urethral obstruction cases, 28 out of 40 patients had a body condition score ranging from 6/9 to 9/9.

Imaging examinations have highlighted significant aspects, especially in urethral obstruction, where the presence of pelvicaliectasis and perivesical fluid is closely associated with the severity and duration of obstruction, correlated with the presence of azotemia and severe hyperkalemia.

Analyzing the microbial landscape of urinary tract infections, a predominance of Gram-negative bacterial species was observed in both dogs (69.44%) and cats (79.16%). Out of a total of 84 bacterial strains isolated, 25 strains (29.76%) showed resistance to at least three classes of tested antibiotics. Among these, 2.38% exhibited resistance to all tested antibiotic classes. Furthermore, the susceptibility profiles of bacterial strains varied significantly, with Gram-positive strains demonstrating different degrees of resistance to certain antibiotics, while Gram-negative strains exhibited extended resistance to multiple agents. Comparing the results of this study with those reported in studies from different geographic areas revealed considerable variability in antibiotic resistance, emphasizing the need to understand the local profile of bacterial sensitivities and resistances for appropriate treatment selection.

The therapy of uropathies requires a multimodal approach, integrating various therapeutic modalities such as medication therapy, medical nutritional therapy, antimicrobial therapy, and surgical therapy. The importance and effectiveness of diet were emphasized in the case of cystoliths, where the complete dissolution of an 8.2 mm calculus in a cat was achieved in 206 days (6 months and 23 days), with periodic ultrasound monitoring and adjustment of treatment based on the patient's needs at that time.

**Keywords:** cystitis, bacteriuria, ammonium-magnesium phosphates, cystoliths.