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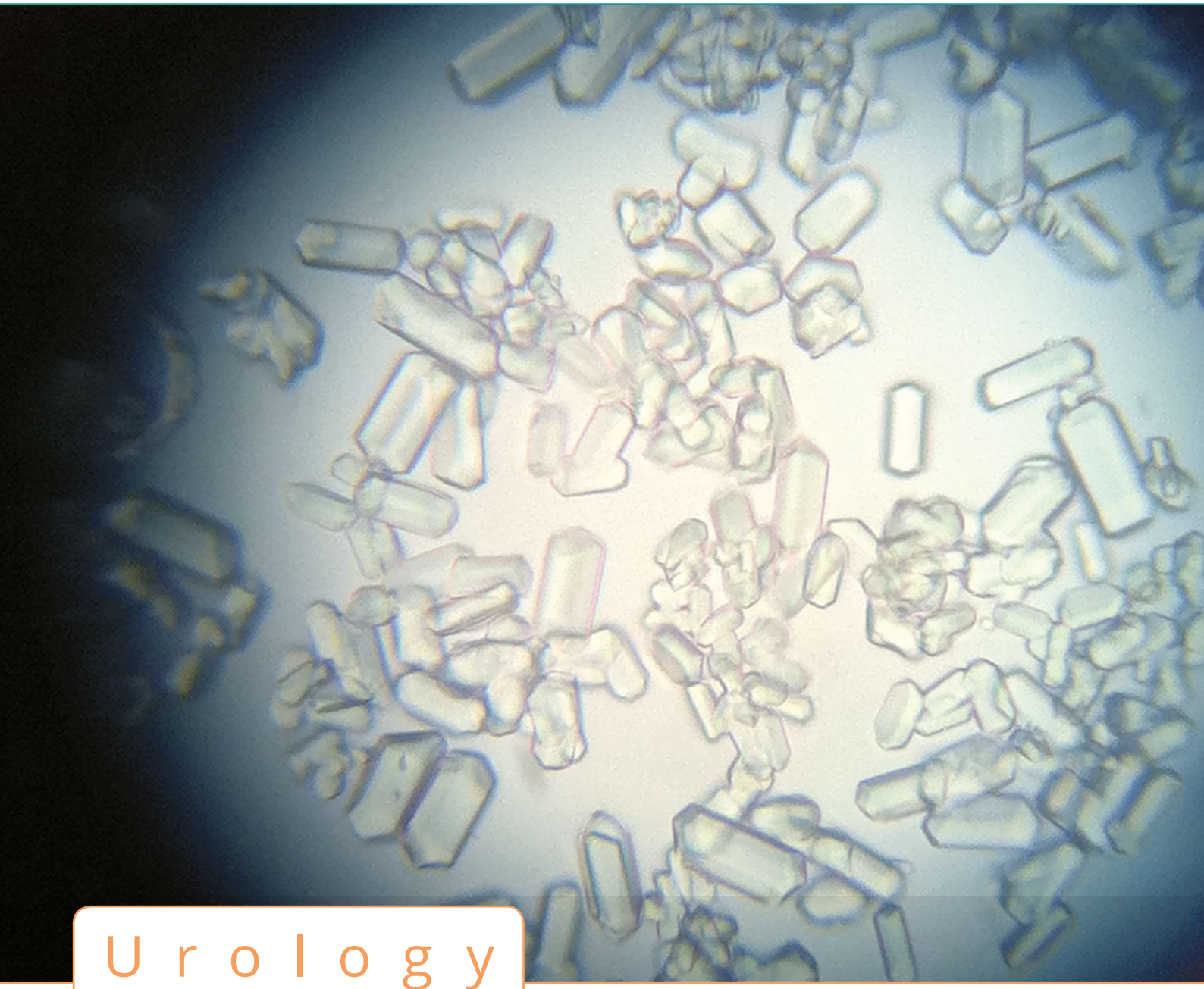

Urology

Bilateral ectopic ureter of a dog with hypoplasia of the kidney.

Difficulties in the treatment of patients with end stage renal disease (stage 4 according to the IRIS criterion).

Nodular dermatofibrosis and renal cystadenocarcinoma in German pointer.

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Dear Readers!

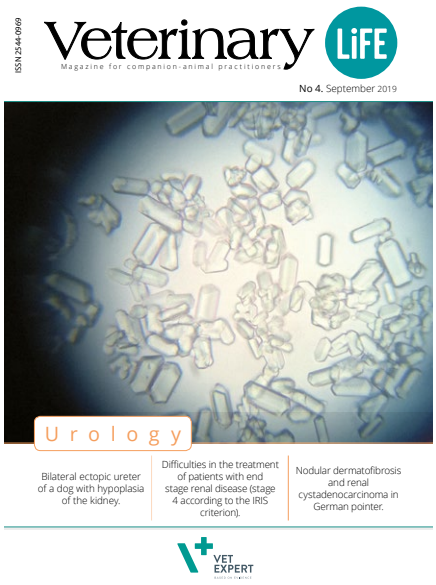
Diseases of kidneys and urinary tract in dogs and cats have already become a real plague, and their diagnosis for most patients means a necessity of long-term treatment, sometimes for the rest of their lives. Statistics from veterinary practices indicate that every tenth dog and every third cat has nephrological disorders. These diseases can have a primary character, but also often are a symptom of other systemic diseases.

The treatment of diseases of the urinary tract also includes, in many cases, a proper dietary treatment. In that way, we are able to stop or to slow down the development of kidney failure or to completely eradicate the calculosis of the urinary tract. The proper diagnostics is also very important, since a quick and accurate diagnosis can mean several additional months or years of life for a patient. Determination of appropriate indicators in blood plasma and imaging tests of the urinary system became a standard way of dealing with the problem at most veterinary surgeries.

To meet the interests of our clients and veterinarians, we have devoted this issue of "Veterinary Life" to the urology. In this edition, we present some interesting clinical cases in cats that are more exposed to urological problems, as well as cases in dogs. Personally, I encourage you to read the clinical article by a veterinary surgeon Anna Klimczak regarding nodular case of dermofibrosis and renal cystadenocarcinoma in case of a German pointer.

Enjoy the read!

Anna Rutkowska
Redaktor naczelna



Veterinary LiFE

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Feline idiopathic cystitis

The general term feline lower urinary tract disease (FLUTD) describes a syndrome characterized by pollakiuria, stranguria, hematuria, and/or inappropriate urination, and it doesn't refer to a specific disease of the lower urinary tract [1-6]. Feline idiopathic cystitis (FIC) is one of the most common causes of lower urinary tract signs in cats, and is the leading cause of FLUTD in young cats. The pathophysiology of FIC is complicated and not completely understood. It is likely that FIC is not a disease entity itself but rather a syndrome that appears to involve abnormalities in many body systems, including the nervous system, hypothalamic-pituitary-adrenal axis, and the bladder. Central nervous system abnormalities associated with increased sympathetic nervous system activity are believed to play a pivotal role in the pathophysiology of FIC, and bladder lesions might just be the result of these nervous system abnormalities and not the actual cause of the disease. Diagnosis of FIC is typically a diagnosis of exclusion, and treatment is based mainly on symptomatic and supportive measures in association with appropriate environmental modification.

Pathophysiology

The underlying cause of FIC remains unknown, and given the variety of clinical manifestations, it is more appropriately characterized as a syndrome rather than a single disease entity. There are growing evidence that simultaneous local bladder abnormalities and neuroendocrine alterations play an important role in the pathophysiology of FIC.

Current studies focus on urothelial permeability abnormalities in cats with FIC, as has been shown in human idiopathic cystitis [13, 14]. Normally, the bladder wall mucosa contains glycosaminoglycans (GAGs) and glycoproteins, preventing urine leakage through the urothelium. Studies in cats with FIC have demonstrated the presence of decreased concentrations of bladder wall GAGs [15-17]. This, in combination with the frequent urination of small urine volume and the altered permeability of potassium ions from the disturbed epithelial barrier seen in cats with FIC, leads to frequent contact of highly concentrated urine with the uroepithelial tissue and the stimulation of sensory nerve fibers of the submucosa, respectively. In addition, various environmental factors can alter the frequency of urination such as frequency and amount of water consumption, reduced mobility, dirty and few available litter boxes, thus contributing to the pathophysiology of FIC.

Stress seems to play a central role in the pathophysiology of FIC. There is the theory that chronic stress in susceptible cats leads to increased stimulation of sensory nerve system and changes in the permeability of the urothelium. Consequently, in cats with FIC, the response of the hypothalamic-pituitary-adrenal axis is characterized by excessive catecholamine release and decreased cortisol response. Recent studies have shown that cats with FIC have smaller adrenal glands, increased plasma catecholamine concentration, and increased urothelium bladder permeability compared to healthy cats [18, 19]. Considering all the above, it is clear that FIC does not result solely from alterations that occur locally in the bladder but involves complex interactions between various body systems.

Risk Factors

Several studies have investigated potential risk factors for the occurrence of lower urinary tract signs in cats, but often without differentiating the underlying cause [6-10]. Reported risk factors in cats diagnosed with FIC include [2, 11, 12]:

- young to middle age (peak occurrence 2 to 7 years with a range of 1 to 10 years)
- neutering
- indoor housing
- use of a litterbox for urination and defecation
- obesity
- diet consisting of >75% dry food
- decreased water intake
- stressful conditions (e.g., recent moves, owner travelling for several days)
- multi-cat household
- poor environmental enrichment .

Clinical presentation

The clinical presentation of cats with FIC is indicative of feline lower urinary tract disease (FLUTD) and is not specific for FIC. Presenting clinical signs include one or more of the following:

- Inappropriate urination (periuria). Cats with FIC are often urinating outside

the litterbox and this is one of the most common (and often the only) clinical signs of FIC.

- Stranguria
- Pollakiuria
- Hematuria
- Dysuria (often with vocalization).

Clinical signs may be acute or chronic (recurrent). The development of clinical signs typically requires predisposition of the animal (internal factors) in association with external factors such as stressful events. However, external stressful events are not always identified. Clinical signs of FIC typically spontaneously resolve in <7 days, even without treatment, but in >50% of cats, clinical signs will recur within 1 year of the initial episode. Urethral obstruction (obstructive form of FIC) can complicate FIC in male cats.

Diagnostic approach

Extremely important in the diagnostic investigation of FLUTD is the prevalence of each pathologic condition leading to lower urinary tract signs in different age groups. FIC accounts for 60 to 70% of cases of lower urinary tract signs in cats <10 years of age. In comparison, urolithiasis accounts for 10-20% of cases, while urinary tract infections (UTIs) are rather uncommon (2%) in this age group. In contrast, in cats that present with the first episode of lower urinary tract signs at >10 years of age, FIC is the cause in 5% of the cases, while UTI is the main cause in this age group (50% of cases).

Based on the high prevalence of FIC in young cats, a detailed diagnostic evaluation is typically not necessary in young cats experiencing their first episode of FLUTD. A detailed clinical, nutritional and behavioral history with information on duration and locations of inappropriate urination, volume of urine, number of cats in the household, type of diet (dry versus canned), number of litterboxes and cleaning schedule etc should be taken. Physical examination findings of non-obstructed cats with FIC is typically characterized by a small bladder, the palpation of which might reveal pain or the presence of a thickened wall. A urinalysis should be performed in all cats, and often reveals hematuria, while there is no evidence of UTI. Abdominal radiography and/or ultrasonography may be used to exclude urolithiasis and neoplasia, and a blood culture can be used to exclude UTI if deemed necessary.

General therapeutic approach and management

In most cats with the non-obstructive form of FIC, clinical signs resolve within to 7 days without any intervention [12, 20, 21]. However, owners should be informed that relapses occur in >50% of cats within 1-2 years after the first episode [21]. The goal of treatment during an acute episode of FIC is to decrease the severity and duration of clinical signs, while the goal of chronic treatment between episodes of FIC are to increase the interval between episodes of active disease (flares) in cats with recurrent FIC and decrease the chances of obstruction in male cats. This is done by modifying or eliminating internal and external risk factors for FIC. Because modification of internal risk factors (such as central nervous system susceptibility) is difficult to impossible, the management of FIC is mainly based on modification of external risk factors.

Management of acute episodes of FIC

The management of cats during an acute episode of FIC is symptomatic. The use of analgesics may be beneficial for pain relief, although it is not known if these drugs have any effect in the long-term management of FIC. Pain relief is typically achieved with the use of opioids (e.g. buprenorphine, butorphanol) and/or non-steroidal anti-inflammatory drugs (NSAIDS; e.g., meloxicam). However, there are currently no controlled clinical trials evaluating the effectiveness and safety of either opioids or NSAIDS analgesics in cats with FIC. Buprenorphine (0.01 – 0.02 mg/kg, orally, every 6-12 hours) or butorphanol (0.2 mg/kg, SC, every 2-6 hours) are commonly used for pain relief in cats with FIC, although the latter is not as potent as the former and requires more frequent administration. The efficacy and safety of NSAIDS have been questioned in cats with FIC and should be used with caution in these animals; chronic use should be avoided. Sedatives, such as acepromazine (0.05 mg/kg SC every 8 to 12 hours), may also be used to reduce stress in cats with FIC.

Multi-modal Environmental Modification (MEMO)

MEMO is the most important component of long-term management of cats with FIC and should be considered before other long-term treatments (e.g., medical treatment) are instituted. The recurrence and severity of clinical signs in cats with FIC are reduced with MEMO. It includes a series of appropriate modifications in the environment of the cat that aim to reduce the stress associated with specific environmental factors. Such modifications include, but are not limited to [26, 27, 28, 29]:

- Improvement of interactions between the affected cat and other household members or pets
- Sufficient number (number of cats in the household plus one) of clean litterboxes in quiet, easily accessible places
- Increase in water intake in order to produce more dilute urine. Very concentrated urine may be irritating to the bladder. Feeding canned food, adding water to the food, having several sources of clean fresh water, are some options.
- Promote playing by providing toys that endorse behavioral practices in the wild.
- Pheromone therapy
- Possible exposure to the outdoors.

Drug therapy

Tricyclic antidepressants, such as amitriptyline (5 to 12.5 mg per cat per day), may be used in cats with recurrent or persistent signs of FIC [30, 31]. Long-term use of amitriptyline in cats with FIC could be useful in cases of frequent recurrences of non-obstructive episodes, regardless of the application of more effective long-term treatment methods such as multimodal environmental modifications and specific nutritional management. Clomipramine is another TCA that may be used in cats with refractory FIC at a dosage of 0.25 to 0.5 mg/kg PO every 24 hours. GAG supplementation has not been shown to be of benefit in cats with FIC. Importantly, bacteria do not play a primary role in the pathogenesis of FIC and antibiotics are of no value in cats with FIC unless it is complicated by other factors.

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Urine test is a seemingly quick and easy examination, which can provide us with valuable information about the patient's clinical condition and the functioning of the whole organism. Urine test is one of the most frequently performed tests in veterinary medicine, a cheap and relatively easily available examination. What is important, it is completely painless for the animal, due to which the owners like it. Urinalysis allows the doctor to assess the functioning of kidneys, urinary pathways and urinary bladder. From the urine, we can also get valuable information about endocrine, parasitic or cancer diseases.

Urine test is seemingly very simple, but to be reliable, you need to remember a few things.

Urine collection and storage of a sample

Taking a urine sample from dogs usually does not cause much problem for the owner, whereas in case of cats it can be different. As with people, the first urine of the day is the best to test, i.e. taken during the morning walk. However, it is worth remembering that the key to obtain a reliable result is the time from collection to examination, which is why I personally assume it is best to ask the dog owner to take urine during a walk on his way to the clinic. We have to take into account that not all the clinics are open from the early morning hours, additionally, taking into account the time of receipt of the sample by the laboratory, the time of transport to the laboratory and the speed of analysis in the laboratory (of course, if we perform an on-site examination in the clinic, the time is much shorter). So, it is optimal to designate to your customers the moment of taking a sample which is the most convenient. If we cannot provide a sample immediately after urinating, the owner should be sensitized to keep the sample in the refrigerator (no longer than 4-6h, remember to include the time mentioned in the previous sentence). In case of cats, the "field" is a bit narrower, the cats can do everything not to urinate when we need it most. A frequently used and reasonably effective method is to leave an empty, dry cuvette, which was disinfected by treating the surface with boiling water, and then collect the urine into a syringe or a special container. I strongly sensify that I would not agree to bring urine in jars or containers for food, even if the owner swears that she/he washed and scalded the package – believe me, in such cases literally miracles can be obtained in the results. The urine container can be bought at any pharmacy or ordered from a veterinary

Urine test in cats – a simple study that covers many secrets.

Natalia Jackowska-Pejko DVM, Specialist in Veterinary Laboratory Diagnostics
Vet Planet Sp. z o.o.

wholesaler and given to the customers, it can help avoiding a lot of problems. Unfortunately, some cats do not want to "settle" their needs in an empty litter box. In this case, the solution is a special cat litter to collect urine. Urine collected this way, contains some amount of impurities that the doctor has to take into account for interpreting the result, but it is not a big problem. I have not seen any urine from a dog or a cat that does not contain any contaminants at all (except taken by the puncture). There are very stubborn cats from which we are not able to get urine at home, so we have to massage urine out of the urinary bladder – but the cat must have a relatively mild temperament; this is not a painful procedure, yet it is certainly not the most pleasant one. Ideal for testing is urine collected by bladder puncture – a treatment of low pain and difficulty, however, arouses some resistance among veterinary surgeons.

One should remember that catheterisation in dogs or cats is not too fortunate, for the reason of only urine collection. We introduce the bacteria from the urethra into the bladder which can result in infection. In my opinion, this treatment should be avoided as much as possible.

Basically, we should divide the urine tests into two groups: urinalysis and additional urine tests. Let me start with the research that is done most often. We divide the general urinalysis into three stages: initial (organoleptic) assessment, physicochemical examination (strip + determination of specific gravity) and urine sediment analysis.

Urine test stages
Initial assessment

Evaluating the color and transparency of urine is the first thing we do with the sample. This initial assessment may lead to suspicions of some diseases: dark coloration as a result of babesiosis or poisoning, very clear and transparent urine may suggest polyuria accompanying numerous diseases. Normal urine from a cat is usually transparent, from light yellow to yellow. In a dog, the urine may be pale yellow to dark yellow and most often slightly turbid or cloudy. Urine of other species of animals may be completely different, e.g. the horse urine is cloudy, yellow and foamy, in guinea pigs or rabbits it is cloudy, yellow but sometimes it takes on the whitish color, still within the normal range. Urine is stained to the right color by the pigment known as urochrome.

Physiochemical properties of urine:

Specific gravity of urine (relative density) (SG) – the test is carried out using a densitometer or refractometer. Reading the specific gravity from the strip is an error. Specific gravity is a helpful parameter in the evaluation of many diseases, as many endocrinopathies run with polyuria/polydipsia (PU/PD) which has an effect on urine density. It happens that in addition to PU/PD, the results of a clinical trial and even additional tests remain within the normal range. In this case, the initial diagnosis of PU/PD raises the suspicion of diabetes insipidus, psychogenic excessive thirst, rarely adrenal hyperactivity or renal failure without azotaemia. In healthy dogs, SG shows daily variations (even from 1,006 to 1,040), therefore, in dogs it is important to confirm a low SG by testing several samples taken at different times of the day, even for several days. In cats, such daily fluctuations are not observed, but it can happen, escpecially in cats from which it took a long time to take the sample for examinantion. In such cases the SG may be surprisingly high, which results from excessive urine compaction.

Increase in urine specific gravity indicates:

- Dehydration,
- hemorrhage (internal and external),
- some heart diseases.

Lowering of urine specific gravity indicates:

- kidney failure,
- overactive or underactive adrenal cortex,
- liver failure,
- overactive thyroid gland,
- diabetes insipidus,
- medicines,
- psychogenic.

Urine pH (pH) – urine pH is affected by the type of food given. In herbivorous animals, the urine is alkaline, in the carnivorous ones it is acidic. In dogs and cats, urine should be slightly acidic . Changing the pH of the urine to alkaline can be observed in phosphaturia and bacterial infections. Neutral urine or alkaline urine in carnivorous animals is abnormal and should be acidified (by change of diet, supplements, medicines). In alkaline and neutral urine, it is easier to precipitate crystals that make urination more difficult and painful.

The correct pH of urine depending on the species:

dogs 5.5 - 7.0

cats 5.5 - 6.5

guinea pigs 7.0 - 9.0

Table 1. Urine test, stages

Strip test	Sediment test	Refractometer test
Colour	Sediment	Specific gravity
Clarity	Leukocytes	
pH	Erythrocytes	
Protein	Mucus	
Glucose	Bacterial flora	
Ketones	Epithelia	
Bilirubin	Casts	
Urobilinogen	Crystals	
Hemoglobin		

cattle 7.0 - 8.0

horses 7.0 - 8.0

Protein – the color reaction on urine strips occurs mainly with albumin. There should be no protein in normal urine (a trace amount is acceptable). The appearance of larger amounts of protein in the urine (proteinuria) should be controlled. The main protein appearing in the urine is albumin (albuminuria). Proteinuria may be renal and non-renal. Non-renal proteinuria is usually associated with inflammation or haemorrhage in the lower urinary tract. It also happens that too much sperm in the field of vision (in dogs) overstates the protein level in the urine. Changes in the urine sediment most often indicate the cause. Renal proteinuria primarily arises due to glomerular damage. Each positive result above one + on the test strip should be verified by biochemical examination to precisely determine the level of protein in the urine. Proteinuria should be interpreted in conjunction with the result of specific gravity. If the urine tested has a high specific gravity, the protein at the trace level or one + is not a deviation. Prerenal proteinuria, post-renal proteinuria and renal inflammation can usually be differentiated based on the history and outcome of urinary sediment. Renal proteinuria caused due to abnormal resorption in the tubules is accompanied by glycosuria and abnormal elimination of electrolytes, which makes it possible to distinguish between tubular and glomerular proteinuria.

Hemoglobin – Hemoglobin – normal urine does not contain hemoglobin. The presence of hemoglobin in the urine is called hemoglobinuria. Hemoglobinuria should be differentiated with myoglobinuria, which can also change the color of the urine – while with hemoglobinuria the urine is pink, in case of myoglobinuria the color of urine is unchanged. The appearance of blood in the urine (hematuria) causes the urine to cloud. Hematuria easily differentiates from hemoglobinuria by centrifuging urine, with hemoglobinuria the urine will retain a red hue, with hematuria the blood cells will be in the sediment, and the urine on the sediment will have a yellow hue. The actual hemoglobin appears in the urine at the endovascular breakdown of erythrocytes and the release of hemoglobin to the plasma. Hemoglobinuria only appears when the erythrocyte decay in the vascular lumen exceeds the body's ability to convert hemoglobin to bilirubin. Therefore, in many patients with hemolytic anemia, we do not observe hemoglobinuria, but bilirubinuria, whereas the plasma and serum are icteric.

Table 3. Types of proteinuria

Types of proteinuria	Possible cause
Physiological	*physical effort
	*fever
	*epilepsy
Extravasation	haemoglobinuria & myoglobinuria
	genital tract infection
	congestive heart failure
urinary, extrarenal origin	*bladder stones/ urolithiasis
	*infection
	*trauma or injury, hemorrhages
	*cancer
urinary, renal or kidney origin	*glomerular damage
	*abnormal tubular resorption
	*hemorrhage or nephriti

Causes of hemoglobinuria:
- babesiosis,
- poisoning,
- some medicines,
- some food colors.

Causes of hematuria:
- Renal:
  - pyelonephritis,
  - acute and purulent inflammation of the kidneys,
  - glomerulonephritis,
  - urolithiasis,
  - polycystic kidney disease,
  - toxins.
- Urinary bladder, ureters, urethra:
  - infections,
  - urolithiasis,
  - cancer,
  - parasites (Capillaria plica),
  - inflammation (idiopathic cystitis of cats).
- Reproductive system:
  - cancer,
  - trauma,
  - infection,
  - prostate hypertrophy,
  - prostate cysts,
  - pyometra,
  - estrus.
- Other:
  - Heat stroke,
  - DIC.

Bilirubin – normal urine should not contain bilirubin. Traces of it may appear in the urine of dogs, especially in males of this species. The presence of bilirubin should correlate with the result of specific gravity. With a specific gravity of >1,020, the trace or presence on one + may be within the normal range. The presence of bilirubin at one + at a weight of <1.020 raises the suspicion of clinically relevant bilirubinuria. The presence of bilirubin in the urine of a cat is always considered a pathology. In the presence of bilirubin in the urine, bilirubin crystals can be found in the urine sediment.

Causes of bilirubinuria:
- Haemolytic anemia,
- Primary hepatocyte diseases,
- disorders involving cholestasis.

Urobilinogen – is a pigment derived from the metabolism of bilirubin. In the small and large intestine, bilirubin is transformed into urobilinogens. About 20% of these urobilinogens are absorbed into the blood and pass through the liver in the bile, and in the small amount also in the urine. In the case of liver damage or increased breakdown of red blood cells, the liver cannot pick up and process such amount of urobilinogens, hence their excretion in the urine is increased. Urobilinogen is converted in the urine to the yellow dye of urobilin, which gives it color. Normal urine contains trace amounts of urobilinogen.

The increase in urobilinogen concentration can be observed at:
- intravascular hemolysis,
- hepatitis.

Glucose – the strip test detects glucose using glucose oxidase – an enzyme that gives a color reaction with glucose. Urine of healthy animals does not contain glucose. The pres-

Table 2. Specific gravity

Disease	No. of dogs	Specific gravity		proteinuria %	leukocytes (>5 wpw)%	bacteria %
		Average	Range			
central diabetes insipidus	20	1,005	1,001-1,012	5	0	0
psychogenic excessive thirst	18	1,011	1,003-1,023	0	0	0
hyperadrenocorticism	20	1,012	1,001-1,027	48	0	12
renal insufficiency or renal failure	20	1,011	1,008-1,015	90	25	15
suppurative nephritis	20	1,019	1,007-1,015	70	75	80

ence of glucose in the urine (glucosuria) is therefore a pathological phenomenon. Glucosuria always appears when the blood glucose level exceeds the kidney threshold (for dogs 180mg/dl, for cats 280 mg/dl). In cats, strong stress may cause the kidney threshold to be exceeded and the appearance of sugar in the urine, the second cause of "overload" may be excessive supply of glucose-containing fluids. Glucosuria at the normal blood glucose level indicates renal tubule abnormalities, e.g. Fanconi syndrome, drug damage or acquired disease. The most likely cause of the emergence of glucose in the urine is obviously diabetes, the presence of additional ketone bodies increases the likelihood of diabetes. In the diabetic patients' sediment, bacterial and / or fungal infections are often observed, and the presence of fat globules is quite characteristic. It is recommended that the urine of diabetics be regularly transferred to microbiological culture. Monitoring of diabetes treatment should not be based solely on the assessment of glucose in the urine, especially in cats in whom the renal threshold for glucose may change. Each positive result on a strip test should be verified by biochemical examination to precisely determine the level of glucose in the urine.

Ketone compounds (acetoacetic acid, acetone, β-hydroxybutyric acid) should not be present in the urine of healthy animals. Traces appear sporadically in dogs and are associated with long starvation. Ketones appear in the urine of small animals with diabetes, interestingly, ketonuria appears earlier than ketoacidosis. In cows, the level of ketones is very important in the diagnosis and monitoring of metabolic diseases (ketosis).

Urine sediment study

Urine sediment testing is an extremely important stage in urine testing. A seemingly simple test can present quite a few problems even to a very experienced laboratory assistant. In humans, urine sediment is usually a in trace amounts, in animals the sediment is usually bigger (especially in dogs) and can conceal various secrets. Normally urine should be centrifuged at approximately 2 to 2.5000 rpm. The centrifuged urine should be poured off from the sediment with one movement, and what is left in the sample should be mixed, spread on the slide and evaluated microscopically. In order to assess the urine sediment, the field must be darkened as much as possible and the condenser removed. Urine is seen at x100 and x400 magnification. The urinary tract is divided into active (particular, organized) and inactive (without a form, unorganized) sediment.

Active urine sediment (well-adjusted, organized):

Epithelia – there is a small number of epithelia in the urine and they rarely have a diagnostic value. Transient, flat (polygonal) and caudal epithelia are often found in the urine sediment test, but distinguishing them is not easy. Mature flat epithelia often come from the reproductive system. Transient epithelia appear in healthy animals. A large number appears in inflammation as well as from urine collected by catheterization. Nevertheless, observation of epithelia may prove to be crucial in the diagnosis of urinary tract cancers. The image of epithelium can be very changed in massive inflammation. When lesions in the epithelial image are suspicious, a colored preparation is recommended. While in case of inflammation and suspicion of neoplastic disease, the urinary cytology test should be performed after anti-inflammatory therapy.

Renal tubular epithelial cells appear in the urine in:

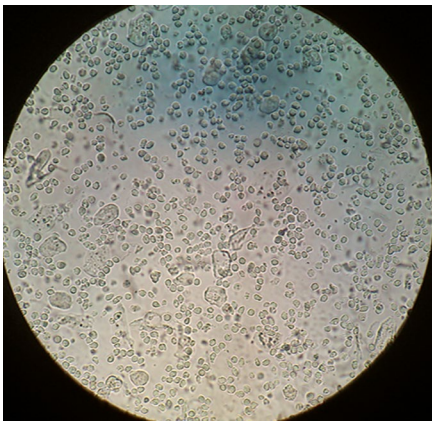
- glomerulonephritis;
- kidney degeneration;
- pyelonephritis.

Urinary tract cells in greater numbers are accompanied by:

- inflammation of the bladder (polygonal and caudal epithelia);
- inflammation of the renal pelvis (caudate epithelium).

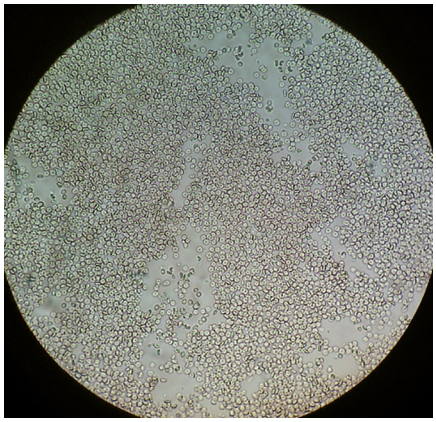
White blood cells (leukocytes) – few white blood cells may be present in the normal urine sediment. The cause of the appearance of an increased number of white blood cells is inflammation or kidney and urinary tract infections. There may be up to 5 leukocytes in the field of vision, properly in the urine sediment. Pyuria is diagnosed solely on the basis of urine sediment analysis, as the strip test is not reliable in dogs and cats and should not be interpreted. It should be remembered that the presence of leucocytes in the urine collected from the micturition may come from both the urinary system and the reproductive system.

Red blood cells (erythrocytes) – may occur in the normal urine sediment as single, fresh red blood cells, up to 5 per high-power field. The appearance of a greater number of erythrocytes indicates bleeding, and the degree of leaching of blood cells indicates the place from which they entered the urine and their residence in the urinary tract. Haematuria may result from lower urinary tract disease (bladder, urethra), upper urinary tract (ureters, kidneys), prostate gland in male or female genital tract, may be the result of inflammation, infection, injury (with crystalluria, catheterization or surgery). It is not possible to precisely determine where the erythrocytes originate from in the urine sediment test, so the study should be correlated with the results of other additional tests and medical history data. In the picture of red blood cells, and hence the quality of the study, time is of great importance, so it is important that the time from collection to examination is as short as possible.



Picture 1.
White blood cells

Casts – a small number of hyaline and granular casts may appear in the urine of healthy animals. A larger number is a pathological phenomenon. The casts are formed in kidneys, so their presence in the urine indicates a disease in the kidneys. Depending on the type of material from which it was formed, the casts can be divided into: hyaline casts containing only protein are transparent and reflect light, cellular casts – in addition to protein they contain cells, which are incorporated in a protein matrix, if they are erythrocytes – the image indicates the bleeding, if they are leukocytes, the inflammation of the kidneys is suggested. The cellular cast is rarely found in the urine as it rapidly disintegrates, the disintegrating cellular casts can form the granular casts (partial disintegration) which are more often found, and waxy casts (total disintegration).

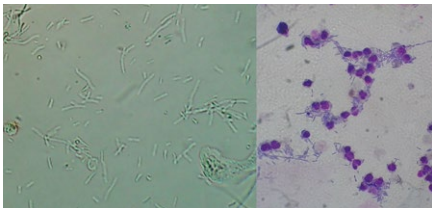


Picture 2.
Red blood cells

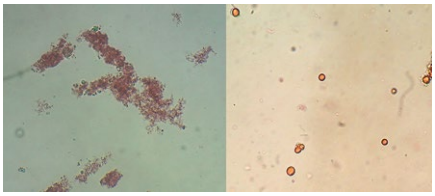
Other components of the urine sediment are bacteria, fungi, parasites, protozoa, and sperm.

Only a few bacteria can be present in the urine collected from the dog and cat.

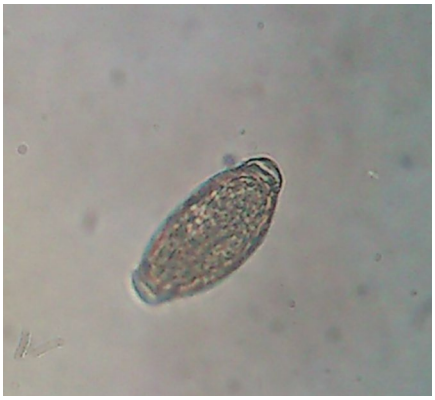
The number of bacteria observed in the urine sediment is influenced mainly by the time from collection to examination. The presence of only bacteria without other inflammatory traits usually results in the proliferation of urine in the bacterial sample and does not indicate a problem in the bladder. There are cases when in the description of the



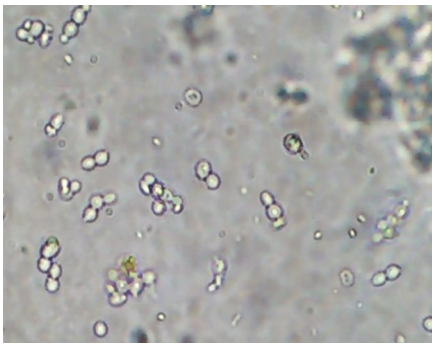
Picture 3.
Bacteria



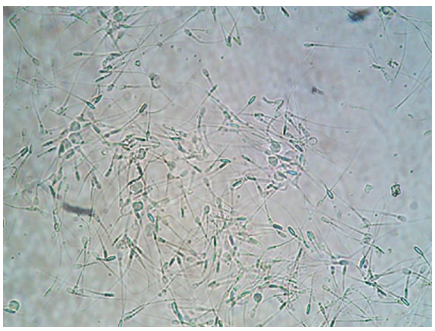
Picture 4.
Fat



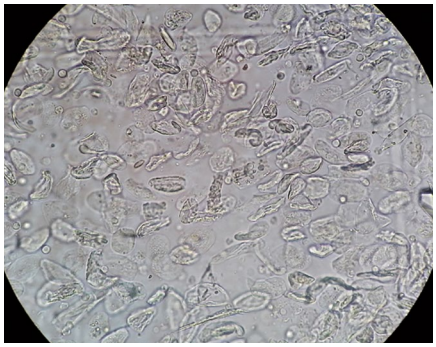
Picture 5.
Capilaria plica



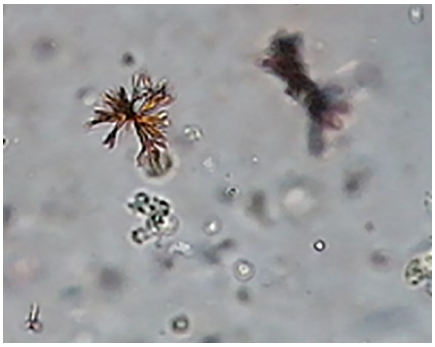
Picture 6.
Fungi



Picture 7.
Sperm



Picture 8.
Epithelial cells



Picture 9.
Bilirubin

sediment we find the information "abundant / large bacterial flora", however, the urine in the microbiological test is sterile. Only the presence of inflammatory traits (leukocytes) and the presence of bacteria should prompt us to collect and investigate the culture of urine. In the case of suspicion of bacterial cystitis, urine is best taken from the bladder puncture. If we do not have the ability to quickly send a sample to the laboratory, we can send urine on the transport-growth medium (Uromedium) used for direct urine culture (available at pharmacies or veterinary wholesalers).

Inactive urine sediment (unpolluted, unorganized), crystals:

Different types of crystals are formed in the urine depending on the concentration of mineral compounds contained in the crystals and the pH of the urine (individual types of crystals show variable solubility at various pH). Very generally, the following differentiation can be made:

- in the acidic urine calcium oxalates, uric acid, amorphous urines, tyrosine, cystine, leucine, sulfonamides, xanthine, bilirubin may crystallize
- in neutral urine, usually there are the same crystals as in acidic pH urine
- in alkaline urine, ammonium-magnesium phosphates (also in the 7 and 6,5), calcium carbonates, calcium phosphates, magnesium phosphates, ammonium urate crystallize.

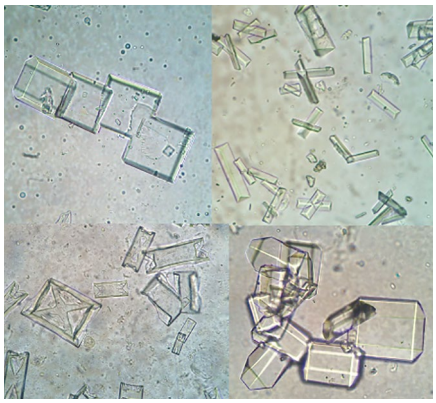
Most crystals have a fairly distinctive look and can be distinguished without major problems. However, there are situations where the correct classification requires an attempt to dissolve the crystals present in the urine.

Ammonium-magnesium phosphates (struvites) – the most common crystals appearing in the urine of dogs and cats. They have a characteristic shape of coffins. In cats, struvites are often observed as the only deviation in the urine sediment analysis. In dogs, struvites most often accompany urease-secreting bacteria.

Calcium oxalates – have a very characteristic appearance of envelopes, less often take the form of an hourglass. They refract light strongly. This type of crystals is considered insoluble and result from diets, drugs or sup-

Table 4. Crystal dissolution

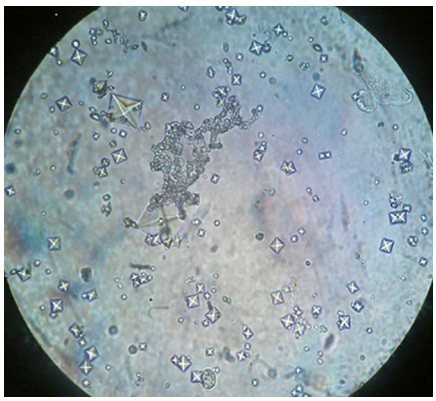
Sediment	Ogrzewanie do 60°C	10% kwas octowy	12,5% kwas solny	15% wodorotlenek potasowy	Aceton
Uric acid	+	-	-	+	-
Urate	+	+	+	-	-
Calcium phosphates	-	+	+	-	-
ammonium magesium triphosphates	-	+	+	-	-
Calcium oxalate	-	-	+	-	-
Cystines	-	-	+	+	-
Tyrosine	-	+	+	+	-
Leucine	-	+	+	+	-
Bilirubin	-	+	+	+	+
Sulfonamides	-	-	-	-	+



Picture 11.
Tammonium magesium triphosphates

plements. The best method is to try to flush them out of the body. They may appear in the urine as a complication of treatment of struvite crystalluria, as well as with hypercalcaemia or excessive consumption of oxalates.

Ammonium urates – usually are brown or yellow-brown and can form spheres or spherical structures with long, irregular protrusions. They appear in the anomalies of the portal vein, severe liver diseases, and metabolic disorders. This type of crystals is often



Picture 10.
Calcium oxalate

observed in Dalmatians.

Calcium carbonates – form yellow-brown or colorless biscuit or hourglass structures. They physiologically occur in the urine of guinea pigs or horses.

Uric acid – takes the form of colorless crystals in the shape of diamonds, whetstone or rosettes. They occur in metabolic disorders, some cancers (leukemia). They can occur in Dalmatians or French bulldogs, due to the reduced reabsorption of uric acid characteristic of these breeds.

Amorphous urates – as the name suggests, do not have a characteristic shape, they are distinguished from amorphous phosphates by dissolution in an alkaline environment. They often form clusters similar to the casts. They occur in metabolic disorders such as ammonium urates, as well as in fever.

Amorphous phosphates – they do not have a characteristic shape, looking like small grey balls (sand). They appear in the urine with bacterial infections, kidney damage, urolithiasis.

Calcium phosphates – can also form long, colorless prismatic structures, sometimes sharp-edged. These crystals can form larger clusters, e.g. rosettes or needles. They are observed in urolithiasis, urinary tract infections and kidney damage.

Cystines – have a very distinctive hexagonal shape (benzol ring), they are colorless, thin and barely visible. They may appear in some metabolic disorders and acute renal failure.

Crystals can also be formed by some urinary excreted drugs. In dogs and cats, the best-known crystals formed in the urine due to the action of pharmacological agents, include the structures formed by the absorption of sulfonamides. Sulfonamides may precipitate in the urine in the form of needles forming characteristic transparent or brown bunches.

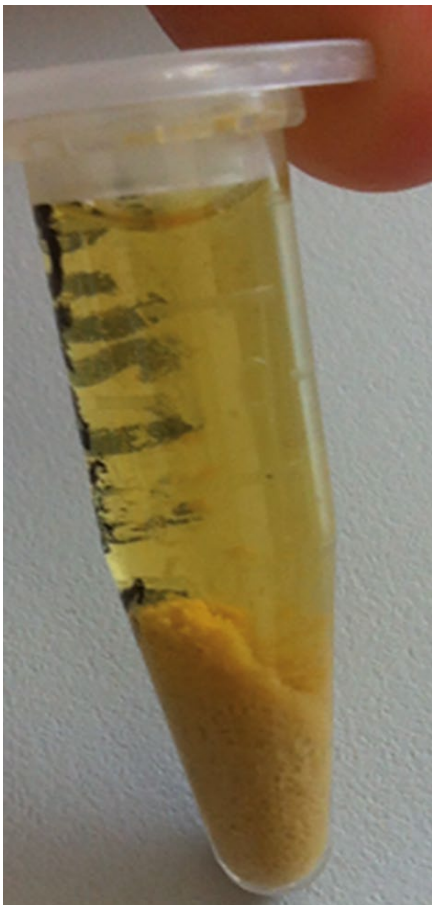
Less frequent components of urine sediment include:

Cholesterol – characteristic plaques appear in:
- fatty degeneration of the kidneys;
- inflammation of the kidney pelvis.

Bilirubin – bilirubin crystals are found in the urine sediment in the course of some liver diseases.

Fat – can appear in the urine in the form of beads, an untrained eye can mistake fat globules with erythrocytes; what definitely distinguishes them is the fact that fat globules have different sizes. However, for special analysis, special Sudan III staining should be performed. Fat droplets appear, among others in the following diseases:
- hypothyroidism;
- diabetes (in dogs, in cats);
- fat cover or overfeeding.

In addition to the general test parameters already described, urine can provide us with much other valuable information. Among the additional tests performed from the urine, one cannot forget about the already mentioned inoculation of urine or urine cytology. In addition, the urinalysis to determine urinary protein creatinine (UPC) ratio provides valuable information on the causes of proteinuria. The correct value of the coefficient is <1. The size of proteinuria is approximately correlated with the cause of glomerular damage. Electrophoresis of plasma proteins and ones contained in the urine may help to identify the source of proteinuria and is helpful in determining the prognosis. The proteinuria induced by hemorrhage has a similar electrophoretic distribution as plasma. Albuminuria indicates early damage to the glomerulus. Hypoalbuminemia and reduced plasma concentrations of higher-mass proteins indicate severe glomerular proteinuria and nephrotic syndrome. The last analysis I wanted to mention is the ratio of cortisol to creatinine in the urine, a test used to exclude hyperactivity of the adrenal cortex (Cushing's Syndrome). It should be remembered that if the correct result excludes hyperfunction of the adrenal cortex, the elevated ratio does not allow to determine the diagnosis.



Picture 12.
Urine sediment

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Potent urine acidifiers in feeding cats

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Struvite urolithiasis is one of the most important causes of feline urinary tract disease (FLUTD). The precipitation of struvite (ammonium magnesium phosphate) crystals is connected with the alkaline pH of urine, therefore all interventions that aim to lower urine's pH to acidic, lead to the dissolution of these uroliths, and the maintenance of acidic urine for a long time protects against the formation of new struvite urolithiasis.

Introduction

Feline urinary tract disease (FLUTD) is one of the more common diseases of adult and elderly cats. From a clinical point of view, however, it is not a disease entity, but a syndrome of clinical symptoms, which in most cases are not specific for individual disease entities included in its composition. In the case of sick cats, the most common symptoms associated with urinary disorders – stranguria, urination outside the cuvette, pain during urination, tightness of urination, hematuria, oliguria, and in the case of urethral obstruction (so-called urethral plugs), anuria. FLUTD can be caused primarily by urolithiasis caused by the formation of crystals and uroliths from calcium oxalate, ammonium magnesium phosphate (struvite), cystine, urate, and also by idiopathic cystitis (FIC). In cats, relatively rarely the cause of lower urinary tract disease is bacterial infection, cancer or anatomical defects. However, taking into account the frequency of individual causes of FLUTD, the most important cause is the struvite urolithiasis and oxalate urolithiasis.

One of the most important differences between struvite uroliths and oxalates is their solubility, because struvite uroliths are soluble in an acidic environment, and oxalate uroliths are completely insoluble. As a result, the identification of urolithiasis in a cat with FLUTD does not allow for the introduction of adequate therapy until the chemical composition of the urolith has been identified. The presence of oxalate uroliths always means the need for a surgical procedure, while the presence of struvite uroliths gives the doctor and the owner the opportunity to start a relatively aggressive diet therapy, which aims to reduce the pH of urine produced by cat and gradually dissolve the urolith, until it is completely eliminated. The key to success, however, is to lower the pH of the urine to make it acidic. Struvite crystals are relatively easily formed at pH above 7.0, while at pH lower than 6.6 they do not arise at all (Finke and Litzenberger, 1992). It is best to keep the urine pH in cats in the range 6.2-6.5, because it helps the process of dissolving already existing struvites, and also prevents the formation of new ones. Of course, such nurtured patients need to be carefully monitored so that the cat's urethral obstruction does not occur during the diet of the cat.

Dietary treatment of struvite urolithiasis

Diet therapy of cats with lower urinary tract diseases is one of the indications for the creation of so-called products of special nutritional use, which are commonly called veterinary diets. In accordance with the Commission Directive 2008/38 / EC of March 5, 2008 establishing a list of planned uses of animal feed for special nutritional needs, it is possible to create a separate diet intended to dissolve struvite uroliths and a separate one to reduce the formation of struvite uroliths. The first one should have the properties of acidification of urine and low level of magnesium. On the label, there should be information on the content of calcium, phosphorus, sodium, magnesium, potassium, chlorine, sulfur, taurine and urine acidifying substance, recommended duration of use is from 5 to 12 weeks; on the instructions for use, information should be provided that the animal should have continual access to water, and on the packaging, container or label, there should be information that it is advisable to consult a veterinarian before use. Diet intended to limit the formation of struvite uroliths differs from the diet intended for their dissolution only in the conent of magnesium, which is to be moderate (and not low), it can be given up to six months, while the instructions do not need to provide information about continual access to water. The other requirements for this diet are the same as for the diet intended for the dissolution of struvites. However, if we look at the composition of these two diets, it is clearly visible that the main requirement for diets fighting struvites is the addition of a substance acidifying urine and reducing the magnesium content.

Potent urinary acidifiers

Potent urinary acidifiers were originally introduced only to dry commercial diets intended for cats with struvite uroliths. Gradually, however, the growing interest in using them also in domestic diets meant that currently some of them are sold on the market in the form of supplementary feeds (dietary supplements) for balancing domestic diets. The popularity of diets for cats with lower urinary tract diseases (including struvite uroliths) has urged various producers and scientists to examine a number of substances which may cause acidification of urine when consumed on regular basis, thus resulting in gradual dissolution of struvite uroliths.

DL-methionine

One of the most often and most commonly used substances to acidify the urine is methionine. The mechanism of its action is based on the fact that the sulfur contained in the molecule of this amino acid is oxidized to sulphates, which are then excreted in the urine and reduce its pH. The results of the studies show that DL-methionine is effective in acidifying urine in cats, when administered in the amount of 3%, but in an amount of 2% is ineffective. It should be remembered, however, that the addition of DL-methionine as a urinary acidifier must be taken into account in balancing the cat's feed ration, because the failure to take this amount of sulfur may lead to a decrease in cat's food intake and possible weight loss of

the cat receiving DL-methionine. Several studies have shown that this decline is transient, but nonetheless noticeable. The efficacy of DL-methionine used in various doses for urine acidification in cats is shown in Table 1. When DL-methionine is administered as a dietary supplement rather than a commercial feed additive, its dose can range from 500 to 1500 mg/cat/day (Abe et al., 1999).

Ammonium chloride

Ammonium chloride is the second, after DL-methionine, substance of choice for urinary acidification in cats. It is effective in diet therapy of feline urinary tract diseases, but in most cases, it must be administered for a longer time. In one of the studies conducted, ammonium chloride fed in a 0.4% dose resulted in a decrease in urinary pH to 6.4, while a 1.1% decrease in urine pH to 5.9. In cats participating in this study, but belonging to the control group, urine pH was maintained at 6.87 (Izquierdo and Czarnecki-Maulden, 1991). However, it should be remembered that urine pH below 6.0 may already indicate acidosis. Funaba et al. (2001) also confirmed the effective lowering of urinary pH in cats receiving ammonium chloride at a concentration of 1.5% for 3 weeks. The dose of ammonium chloride used as the only food additive is 200 mg/kg/day, orally, divided into three doses. The use of ammonium chloride may also contribute to an increased calcium urine release, which in turn may be a factor facilitating the formation of calcium oxalate uroliths.

Other

The remaining urine acidifiers are not considered as effective as DL-methionine and ammonium chloride, but in some cases, they are used successfully. The urine-acidifying properties have, for example, calcium chloride when administered instead of calcium carbonate (Pastoor et al., 1994). Sodium disulphate and phosphoric acid, used at doses from 0.4% to 0.8%, proved to be effective acidulants of urine (Spears et al., 2003). Vitamin C has similar properties of acidifying urine (ascorbic acid) administered to cats at a dose of 400-1000 mg/kg m.c./day (Kienzle and Maiwald, 1998).

Table 1. Urine pH, urine crystals concentration of struvites and daily excretion of struvite crystals to steady during a two-week study of the DL-methionine ability to acidify urine in cats (Abe et al., 1999)

Index	Addition of DL-methionine as a supplement %				SEM
	0	1	2	3	
pH of urine					
Week 1	6.68	6.69	6.67	6.07a	0.24
Week 2	6.82	6.86	6.48	6.12a	0.31
Struvite crystals, number / µl					
Week 1	76.3	154.0[b]	96.5	4.5[a]	42.6
Week 2	195.0	113.7	72.5	2.3[b]	79.7
Struvite crystals, number x 10^{-5}/d					
Week 1	54.4	71.3	43.6	2.4[a]	18.2
Week 2	109.9	52.6	39.4	1.1[a]	38.1

[a]p<0.05 vs. 0%

[b]p<0.10 vs. 0%

Summary

Urine-acidifying substances are used relatively commonly in commercial cat food, owing to which the incidence of struvite uroliths in the cat population has declined significantly in recent years. Increasingly, however, they are also added to domestic pet food for this species of animals, and in this case, it is necessary to observe their dosage, because an excessive amount of DL-methionine or ammonium chloride can negatively affect the food intake and weight of the cat. In addition, there may also be disturbances in the balance of minerals in the urine, primarily associated with increased calcium excretion, which in combination with acidic urine may be a factor conducive to the precipitation of calcium oxalate uroliths.

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Bilateral ectopic ureter of a dog with hypoplasia of the kidney

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Congenital Anomalies of Kidney and Urinary Tract include a wide range of diseases of the urinary system resulting from abnormal developmental processes, such as kidney disorder, abnormal kidney migration, impaired urinary tract development.

Birth defects of the urinary tract are quite rare. They are the main cause of chronic kidney disease (CKD) in animals at an early age.

The introduction of routine ultrasound examination into the veterinary practice contributed to the earlier detection of congenital malformations, and thus to more precise medical management.

Congenital anomalies of the urinary system can be divided into: a) kidney defects; b) birth defects of the ureters; c) birth defects of the bladder; d) birth defects of the urethra.

In the following article, we focus our attention on the defects of congenital upper urinary tract.

RENAL CONGENITAL ANOMALIES

Renal congenital anomalies include kidney agenesis, i.e. the absence of one kidney, resulting in the second kidney undergoing hypertrophy, or compensatory hypertrophy. Agenesis is accompanied by a lack of ureter and part of the bladder triangle. Hypoplasia of the kidney is a congenital small kidney with normal morphology. Kidney dysplasia is a reduced kidney with altered morphology. The cause of innate renal dysplasia is inhibition of the development of nephrons and replacement of them with fibrous tissue during fetal life.

Another congenital anomaly of the kidneys is their innate polycystic disease, which is an inherited disease, more prevalent in cats than in dogs. Polycystic kidney disease is characterized by the appearance of numerous cysts of various sizes. The cysts in the kidneys may be accompanied by cysts in other organs such as the liver or pancreas.

URETER CONGENITAL ANOMALIES

The most frequently diagnosed defect of the ureters is their ectopia (displacement). This defect is related to the disruption during the embryogenesis of the urinary tract, which is located outside the bladder.

The ectopic aspect of the ureter may be of a different nature. The dislocated ureter may be placed intraocularly in relation to the bladder, bypassing the place of the normal ureteral orifice and ending in the neck of the bladder, urethra or vagina. It can also be placed completely outside the bladder (outside the wall) and enter the vagina, uterus, urethra or rectum.

The ureteral ectopic can be single or double-sided. In the case of unilateral ectopia, one should also expect other developmental defects of the genitourinary system, i.e. innate failure of the urethral sphincter or underdevelopment of the urinary bladder.

Dislocation of the ureter is more common in females than in males, and the ureteral orifice of dislocated ureter is most often located in the urethra.

The symptoms of ureteral displacement include urinary incontinence as well as intermittent, recurrent urinary tract inflammation (UTI), ureteral dilatation, hydronephrosis.

DIAGNOSTICS OF THE URETER ECTOPY

In order to diagnose ureteral dislocation, it is not enough to perform ultrasound examination of the abdominal cavity. For this reason, a contrast test is recommended, often combined with pneumocystography. To make a urography (a contrast test of the urinary tract), the patient should be prepared in advance. For this purpose, we carry out a twelve-hour fast and an enema to get rid of residual gastrointestinal contents that could interfere with the interpretation of the radiograph. Fluid therapy is also an important element in preparing the patient for this study. Its aim is to eliminate the negative effect of the contrast agent on the kidneys. The next stage of the study is an intravenous iodine contrast agent with an iodine content of 200-300 mg/dl in an amount of 1-2 ml/kg of body weight in the form of a bolus or a rapid intravenous infusion, followed by X-ray or computed tomography (CT).

An alternative to urography can be endoscopic examination. However, this method cannot always be used in veterinary patients.

TREATMENT OF THE URETER ECTOPY

The procedure of choice is a surgical procedure, and the choice of the method is conditioned by the type of dislocation as well as by the intensity of changes. If ureteral displacement is accompanied by kidney defects or hydronephrosis, the removal of the kidneys (nephrectomy) should be considered, as ureterocystoneostomy will not always be enough to regress hydronephrosis.

OTHER ANOMALIES OF URETERS

The less frequent ureteral defects include their absence, abnormal development or double ureters.

Noteworthy is the ureterocele, or cystic widening of the ureter just around the ori-

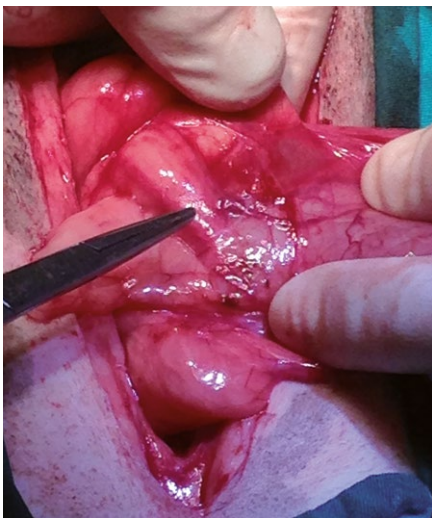

Photo 1a.
Incorrect course of the ureter.

fice. This defect is often the cause of recurrent urinary tract infections (UTI), and may also result in the appearance of hydronephrosis.

Vesico-ureteral reflux is a pathological condition in which urinary bladder retreats to the upper urinary tract. This defect is characteristic of the age of the puppy. The main reason is the incorrect structure or malfunction of the vesico-ureteral junction. This type of disorder may also occur due to high micturition pressure, which is a functional or anatomical consequence.

The cause of the functional obstacle may be overactive bladder detrusor, impulse-sphincter coordination disorder or increased sphincter tension. Among anatomic reasons, defects such as phimosis, hypospadias, ureteral orifice ectopy, ureterocele are distinguished.

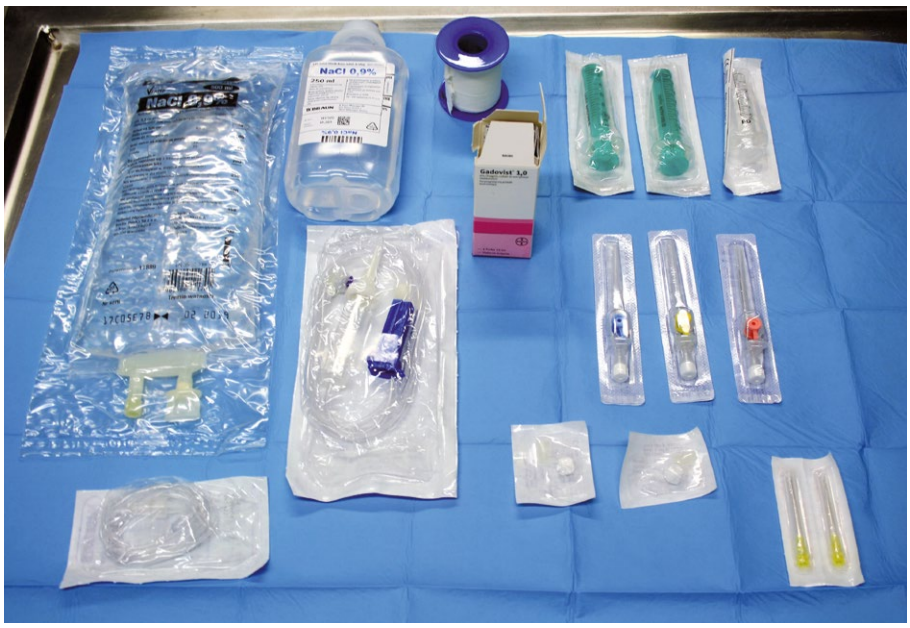

Photo 1.
A set needed to carry out a urography

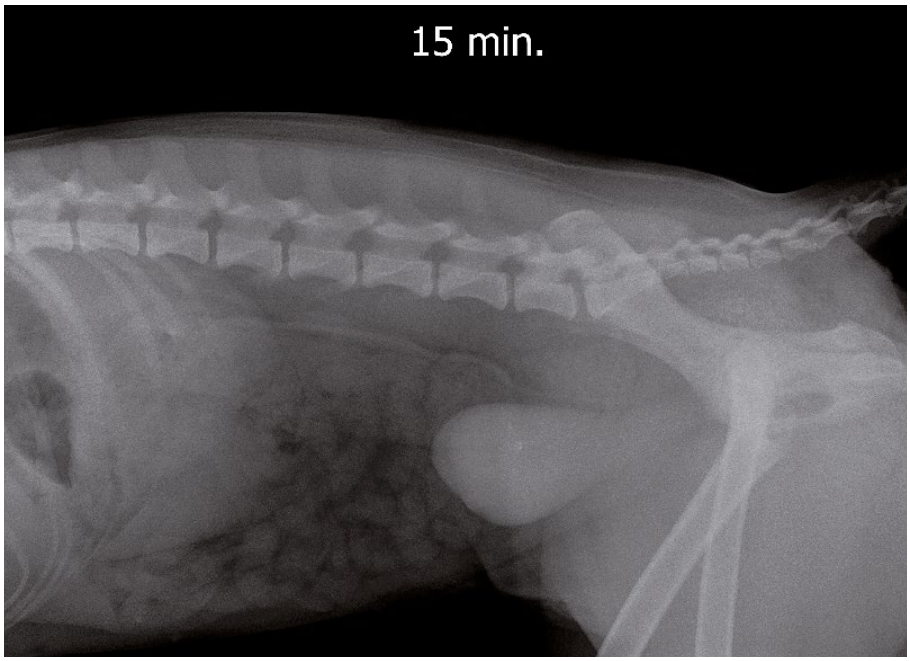

Photo 2.
Contrasted ureter. The location of the ureteral outlet is impossible due to the stagnant fecal mass in the rectum.

A CASE REPORT

An owner with an appenzeller dog came to the veterinary clinic for an nephrological consultation. The cause of the consultation was hypoplasia of the left kidney and symptoms of urinary incontinence. Additional tests, such as a basic urinalysis, determination of urinary protein creatinine (UPC)

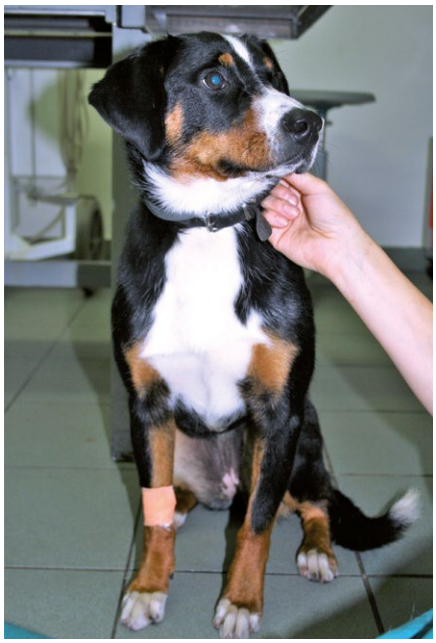

Photo 3.
Patient during the control visit.

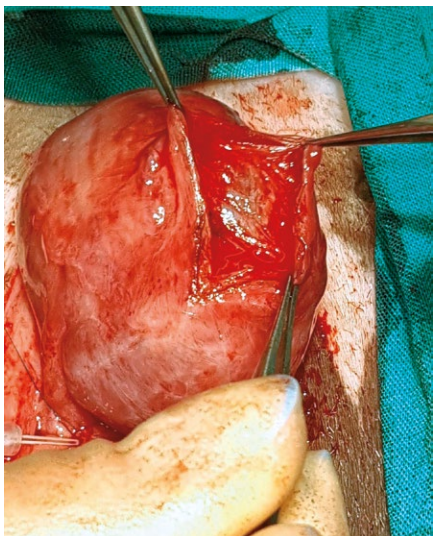

Photo 4.
Lich-Gregoir technique

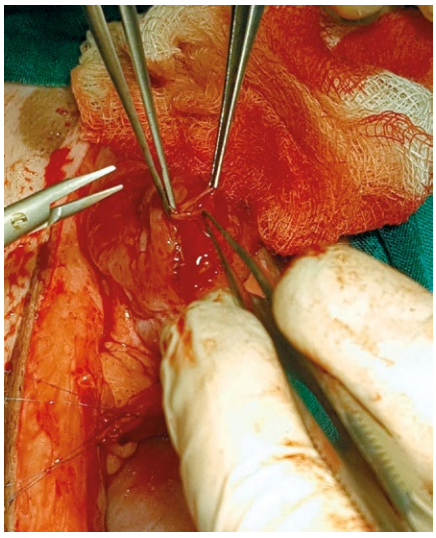

Photo 4b.
Lich-Gregoir technique

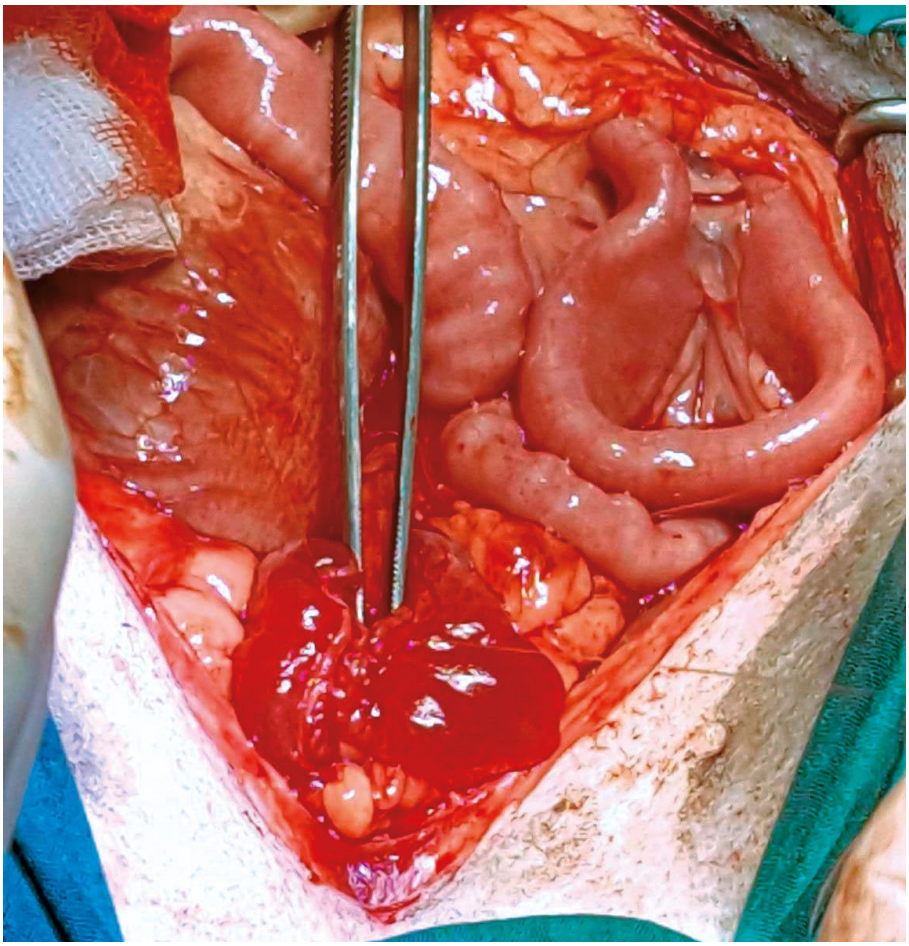

Photo 4c.
Lich-Gregoir technique

ratio, bacteriological examination of urine and ultrasound were ordered. Urinalysis excluded bacterial infection, and ultrasound examination showed widening of the ureter in the left kidney, which led to the suspicion of ureteral ectopy.

The next stage of the diagnosis was the performance of a contrastive urinary tract, i.e. urography. For this purpose, IOMERON contrast agent was used at a dose of 2 ml/kg b.w. and a series of X-ray images were taken. The contrast study revealed an abnormal ureteral orifice, bypassing the orifice to the bladder. Due to the presence of faecal matter in the rectum, it was impossible to determine the exact ureteral orifice.

A decision was made to perform a surgical procedure to correct ureteral abnormalities.

An exp-lap was performed, the access was obtained in the midline, revealing the left ureter, the orifice of which was located behind the neck of the bladder. The ureteral plasticization was performed using the Lich-Gregoir method, based on the reconstruction of the bladder antireflux mechanism.

Then, the evaluation of the right ureter was performed, which also showed an anomaly in its orifice. The plastic surgery of the second ureter was abandoned due to too high risk of complications, which may include hydronephrosis of the kidney, ureters of which have been operated. Therefore, the next procedure was performed within 8 weeks using the same surgical technique of ureteral anastomosis.

CONCLUSIONS

Congenital anomalies of kidney and urinary tract happen quite often. It is very important to carry out detailed tests and accurate diagnostics, because one anomaly does not exclude the other. Depending on the cause of the anomaly, we have a wide range of diagnostics as well as medical treatment. However, we should always be guided by the good of the patient and rationally determine possible complications resulting from our activities.

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Chronic renal failure is a slow-growing disease, which gives the ability to adapt to the deteriorating function of the organ. Nevertheless, like any other chronic disease with progressive "adaptation", this adaptation is temporary. Disturbances in the regulation of calcium and phosphate management are often observed in the course of the disease. In a healthy animal, the function of the "main" regulator is parathyroid hormone (PTH), and parathyroid glands, digestive tract, kidneys and bones participate in the process itself. Lowering Ca concentration in serum and increase in P concentration stimulate PTH production, which intensifies bone resorption of Ca and P, increases reabsorption of Ca in the kidneys, reduces P and activates 1-alpha hydroxylase, which intensifies the production of the active form of vitamin D3. This vitamin improves absorption of Ca and P from the gastrointestinal tract and their release from the bone. The tabulation of Ca and P concentrations by retardation stops the PTH production.

In chronic renal failure, disturbances of the Ca-P metabolism are also explained by the factor FGF-23 (Fibroblast Growth Factor - 23). It is produced by osteoclasts in response to an increase in serum phosphorus. Its function is to stimulate the excretion of phosphorus by the kidneys and to reduce the activity of 1-alpha-hydroxylase. Chronic hypocalcaemia, which is the result of chronic renal failure, considered to be the main cause of secondary renal hyperparathyroidism, stimulates the production of parathyroid hormone (PTH).

This hormone causes the increase of FGF-23 and the inhibition of 1-alpha-hydroxylase, which leads to a decrease in the level of vitamin D3, and this in turn directly stimulates the secretion of PTH by the parathyroid glands. The consequence is the reduced absorption of Ca and P from the gastrointestinal tract, increased bone release and increased Ca-resorption and reduced P in the kidneys. The formation of a Ca-P balance related to the increase in PTH and FGF-23 activity is temporary. Progression

Chronic renal failure and phosphorus in dogs and cats.

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of the disease and constant stimulation of PTH and FGF-23 secretion do not induce further desirable effect of Ca-P balance. An increase in phosphorus concentration, overproduction of PTH and a decrease in ionized Ca concentration are observed.

In addition, FGF-23 factor by inhibiting 1-alpha hydroxylase reduces renal production of active vitamin D3 and increases 24-hydroxylase activity, which can lead to vitamin D3 deficiency. (7). As a result, in the therapy of chronic renal failure in animals, monitoring of the body's Ca-P-management is of great importance, which is primarily associated with an effective reduction in the concentration of phosphorus in the blood. This can be done by introducing a phosphorus-deficient diet and/or using binding agents for this element.

The simplest form of diet is the introduction of a commercial product, depleted in phosphorus (for dogs – less than 0.4% s.m., <0.08 g/100 kcal, for cats – less than 0.5% s.m., <0.12 g/100 kcal). It guarantees a proper balance, stability of parameters and safety of use, and is the most convenient form of sick animals' nutrition for the owner. Another option is to prepare a home-made diet. Nevertheless, it is worth emphasizing that it is much harder to maintain an adequate balance of nutrients in this case. To a large extent it depends on the current content of nutrients in the product and may vary depending on the method of production of raw materials (in the case of meat - the way of feeding animals, in the case of growing plants – e.g. fertilization, etc.), storage and processing technology. Another risk point is the addition of vitamin and mineral supplements, which in most cases worsen the palatability of meals, thus constituting a big problem with an animal with variable or poor appetite. Therefore, very often in the case of home diets vitamin and mineral supplementation is omitted, which in itself distorts the ratio of Ca-P, in favour of phosphorus. Safety of use is also important, and this can be a big problem, especially for raw diets, where cases of bacterial and parasitic poisoning are described.

Phosphorus in the diet may be found in an organic form (products of animal and vegetable origin), mainly related to proteins and inorganic (food additives). The main sources are dairy products (100-900 mg/100 g), meat and fish (200 mg/100 g), liver, eggs, yellow cheeses, peas, seeds, beans, potatoes, whole-grain products (100-300 mg/100 g) and carrots. The organic phosphate in the digestive tract is hydrolyzed to inorganic form before being absorbed. Its absorption occurs in the duodenum (35%), jejunum (25%) and ileum (40%) and ranges from 30 to 60%, depending on its bioavailability, the degree of activation of vit. D3 and the presence of other compounds such as: calcium, aluminum, nicotinic acid. It turned out that nicotinic acid administered to rats with renal insufficiency regulated the expression of the transporter (Na/Pi IIb), responsible for the absorption of phosphorus in the jejunum, as a result of which a decrease in its absorption was observed (4). Similar results were obtained in dialysis patients who had a significant decrease in blood phosphate (11).

When assessing the bioavailability of this element, it should be noted that products of animal origin will be the best source of phosphorus. This is due to its combination with proteins, easy hydrolysis and good absorption. In plant products, phosphorus is bound in the form of phytic acid and phytates, and its availability depends on the activity of phytases (enzymes present in plant products) (12). Their activation occurs, for example, during germination of grains or processes occurring during acidification, therefore the absorption of phosphorus from various products of plant origin is different. The lack of phytases in animal organisms limits the bioavailability of phosphorus from this source to about 10-30%. Therefore, despite the high content of phosphorus in whole grains, seeds and fruits, their effect on the concentration of this element in the blood is limited. This was confirmed by the studies by Karp et al, who evaluated the concentration of phosphorus in the blood serum of people who are on a diet consisting mainly of meat, dairy products, non-fermentable whole grain products and with the addition of inorganic phosphates. Statistically, significantly higher concentration of phosphorus was found in people who were on a meat diet and with inorganic phosphates, in relation to the other two groups (8). A very serious source of inorganic phosphorus are products of the food industry, where this element performs technological functions (preservative, taste and color enhancer, moisture stabilizer, structure and consistency). In this case, the source of inorganic phosphorus for humans is: carbonated beverages, meat preparations, frozen dishes, processed cheese, instant products and bakery semi-finished products (10). Some of them are also found in the dog or cat's menu, which should be taken into account when choosing/balancing a diet for a sick animal. In the studies of Michalski et al., The most inorganic phosphorus (850 mg/100 g) turned out to be in sausages, which owners often serve their dogs and cats as a snack, reward or for administration of a tablet (10) .

In addition to lowering the phosphorus content in the diet itself, with increasing its concentration in blood serum, chelating compounds are introduced into the therapy in animals. The aluminum salts are the oldest and most effective, which at the same time pose a risk of accumulation and high toxicity (13). The standard starting dose is 30 to 100 mg/kg m/day, and after lowering the blood phosphorus level to the desired value,

Table 1. Recommended concentration of phosphorus in blood serum according to the International Renal Interest Society (IRIS)

	The range of phosphorus concentration to achieve depending on the phase of chronic kidney disease	
	mg/dL	mmol/L
IRIS CKD phase 2	3.5-4.5	1.13-1.45
IRIS CKD phase 3	3.5-5.0	1.13-1.6
IRIS CKD phase 4	3.5-6.0	1.13-1.9

it is recommended to reduce the dose to the lowest working dose. However, more often than aluminum salts, calcium salts and/or their compositions with other substances, e.g. calcium carbonate, calcium carbonate + chitosan, etc., are included in the treatment. The recommended dose of calcium carbonate is from 90 to 150 mg/kg day. However, it should be mentioned that this compound binds phosphorus rather weakly, and in addition must be dissolved in the acidic environment of the stomach to work. Therefore, we should take into account the weaker effect of using this chelator with concurrent administration of proton pump inhibitors or H2 receptor antagonists.

Another phosphorus binding compound is an ion exchange resin (sevelamer) that does not contain calcium, aluminum or magnesium and is not absorbed from the gastrointestinal tract. After the addition of phosphorus, it releases chlorine (sevelamer hydochloride) or carbonate (sevelamer carbonate) into the intestinal lumen. This medicine provides better control, calcemia, renal osetodystrophy and calcification of blood vessels, as assessed in dialysis patients (5).

An even more effective means of lowering the concentration of phosphorus is lanthanum carbonate. It is an element belonging to the 3rd scandiac/scands group in the periodic table. In nature, it is rare, mainly in monazite sand. The lanthanum compounds are very effective in binding phosphates in vitro as well as in vivo. Their potency is comparable to the strength of phosphorus binding by aluminum compounds (1). In studies of patients with chronic renal failure, its use reduced the amount of phosphate absorbed by more than 50%. In addition, it was shown that the tested preparation is safe. In experimental animal studies, it was observed that very high doses of lanthanum carbonate of: 2000 mg/kg, did not cause a significant toxic effect, at the same time effectively reducing the concentration of phosphorous in the blood (2.3). However, it is taken into account that the long-term use of such high doses creates the possibility of accumulation of lanthanum compounds in the liver, bones, brain and other organs (9). Up to now, numerous centers in the USA and Europe have performed numerous clinical trials using lanthanum carbonate administered in therapeutic doses in patients in the second, third and fourth phase of renal failure. And besides the effectiveness of action with a lower number of hypercalcaemia episodes and a more significant reduction in PTH concentration, no toxicity effect was observed for this compound (1.6). The veterinary medicine also uses lanthanum carbonate at an initial dose of 30 mg / kg m / day, and its change depends on the obtained target concentration of phosphorus (Table 1).

Generally, the problem of hyperphosphatemia is one of the elements of therapy in chronic renal failure, which is noticed from the very beginning of the implemented treatment. Adequate tackling of hyperphosphatemia and its effects definitely improves the quality of life of breeding animals.

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Despite the fact that renal replacement therapy in ARI therapy in dogs is gaining popularity due to its effectiveness, in the case of its use in cats, we have encountered serious problems. It turned out that the procedures for hemodialysis developed by us and working in dogs are insufficient for cats to perform them safely in these animals. Problems with their safe execution appeared regularly at various stages of dialysis. Therefore, there was a need to systematize these complications, determine the causes and methods of their prevention.

Here are our insights and suggestions for solving particular problems:

Complications occurring during the start of the procedure.

The occurrence of cardiac arrhythmias to stop its activities is noticed here, including when performing activities related to the removal of stoppers from the anticoagulant filling the catheter's channels and rinsing them with NaCl solution 0.9% before the beginning of the procedure. After analysing and consulting with cardiologists, we came to a conclusion that the cause is an impaired blood flow to the vestibule and the associated lack of proper stimulation of its contractility. The solution turned out to be a slow and smooth aspiration and rinsing of the central catheter canals.

The appearance of neurological symptoms during hemodialysis.

The problem was repeated after about 35-40 min of the procedure. These symptoms, as we predicted, were due to the non-aligned syndrome associated with too fast diffusion within the dialyzer.

Despite the use of the smallest available dialyzer with a dialysis membrane area of 0.2 m^2 and blood flow at the level of 2-3 ml / kg body weight, additionally decreased with the periods of dialysis fluid bypass, the level of urea in the blood of dialysed cats was decreased by 70-80% after this time. Since further decrease in the amount of blood flow through the dialyzer threatened the occurrence of blood

Hemodialysis treatment in cats. A challenge for a veterinary surgeon who provides renal replacement therapy.

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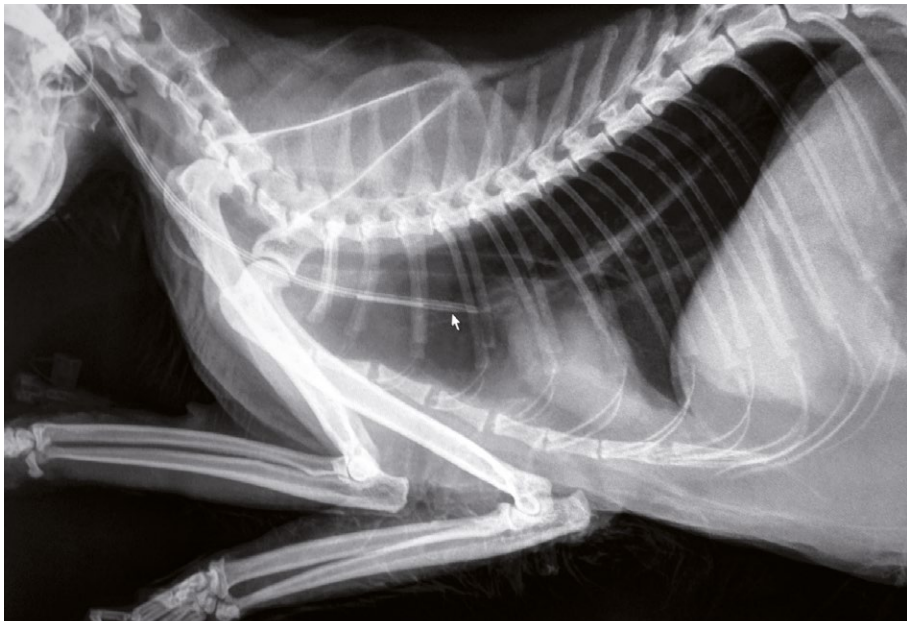

Photo 1.
X-ray showing the location of the central catheter in the patient

clotting in the extracorporeal circulation and related complications, it was necessary to apply an additional mechanism to reduce the intensity of the diffusion process.

We used the possibility of limiting the volume of dialysis fluid flow through the dialyzer space, along with the reversal of its flow direction.

Normally, the dialysis fluid in the dialyzer's space flows in the opposite direction to the blood (contra-rotating system) which has to increase diffusion efficiency.

The concurrent system used by us greatly slowed the diffusion process while being safe due to the clotting of blood flow. This allowed for better control of the diffusion process.

The occurrence of neurological symptoms also led us to suspect that they may be caused by too big changes in electrolyte levels important for the functioning of the nervous system.

The dialysis fluid consists of water, acidic concentrate and bicarbonate treated by reverse osmosis. The adjustable parameter on the hemodialysis apparatus is the level of Na + ions and bicarbonate. It is known that fluctuations in the level of Na + ions can have a significant impact on the function of the nervous system of the patient. In ARI, there is a decrease in the bicarbonate and Na + levels.

During dialysis, we should gradually increase the Na + level, however, not more than 2 mmol/l per treatment. A greater increase in Na+ level may just trigger neurological symptoms.

The conductivity set on the dialyzer is controlled by a system of three conductometers built into the device. We decided to additionally control the actual Na + level in the dialysis fluid. We took it out of the circulation of the dialysis fluid before the dialyzer. The Na + ions level was determined using the ion-selective method using the proLYTE apparatus.

This carefully controlled level of Na + in the dialysis fluid reduced the incidence of neurological complications.

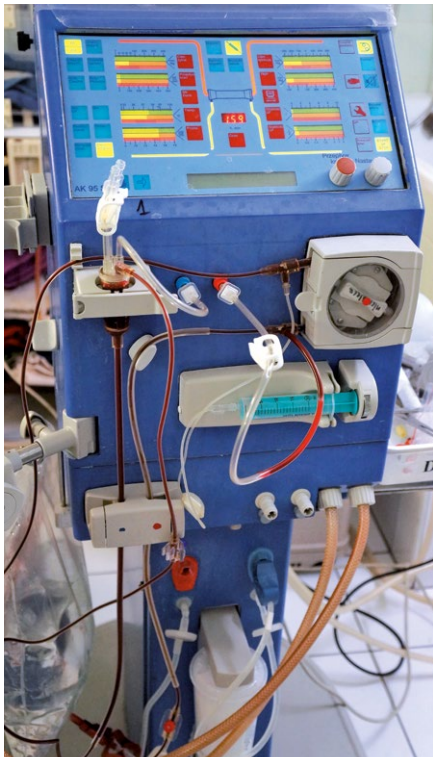

Photo 2.
Armed "artificial kidney" for cat hemodialysis procedure.

Photo 3.
Determination of electrolyte level, ProLyte.

Photo 4.
Preparation of the anticoagulant.

End phase of procedure - rinsing the catheter and securing its channels with anticoagulant.

It turned out that the 46.7% potassium citrate, used by us and perfectly working in dogs, in case it gets in the bloodstream of the patient near the atrium of the heart (even in the smallest amounts), it causes violent cardiac complications.

In cats, it cannot be used. We replaced it with sodium heparin.

All these observations and introduced changes allowed us to perform hemodialysis in cats in a safe and controllable manner. Thanks to this, the cat hemodialysis procedure may be more effective and has the prospect of more frequent use.

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Difficulties in the treatment of patients with end stage renal disease (stage 4 according to the IRIS criterion)

Anna Włodarczyk, DVM

Chronic kidney disease is a state of organ dysfunction over the possibility of physiological compensation. The degree of glomerular filtration decreases and, as a consequence, the accumulation of numerous uremic toxins, the development of uremia, metabolic acidosis and numerous consequences of generalized intoxication of the body occur.

Due to a significant reduction in renal function, the treatment of end-stage renal disease (ESRD), without the possibility of continuous dialysis, must be properly modified to avoid accumulation of medication and even more dysfunctional organ function.

We speak of end-stage renal disease when the creatinine level in blood exceeds 5 mg/dl (440 mmol/l) according to the IRIS (International Renal Interest Society) criterion. In addition, changes in blood pH, hypoalbuminaemia and water management disorders will affect the pharmacokinetics of many drugs.

Simultaneously, acidosis, uremia, hypertension and ionic disorders cause a number of problems that need to be addressed in parallel.

Particular problems will be discussed in the next paragraphs.

Inflammation of the digestive tract

Gastrointestinal problems of cats and dogs are different. In dogs, as in humans, gastrointestinal ulcers are often associated with both elevated gastrin levels in the blood and inflammation. However, in cats the nature of the changes is slightly different - in the histopathological sections taken from the stomach, there were no numerous ulcerations, the main changes were fibrosis and mineralization of the wall. These changes were associated with an increase in gastrin concentration and disturbances in calcium and phosphorus management resulting from nephrogenic hyperparathyroidism (1)

In the case of dogs and cats, the basis of treatment is the use of proton pump inhibitors and H2-receptor inhibitors that lower the pH of gastric juice (ranitidine 0.5-2.0 mg/kg po, iv every 8-12 hours; famotidine 0.5-1.0 mg/kg po, im, iv every 12-24 hours).

Omeprazole is definitely more effective than H2-receptor blockers. The starting dose of omeprazole is 1 mg/kg bw 1/24 hours, although it is reported that single administration may not be sufficient. In justified cases omeprazole can therefore be used every 12 hours.

Ranitidine 2 mg/kg 2 times a day is often too weak and its dosage should be modified and reduced by up to 50 to 75% in the event of a significant reduction in GFR (2.3). Its advantage is the prokinetic action (13).

Cimetidine (5-10 mg/kg po, im, iv every 4-6 hours/dogs) – it works less than ranitidine and famotidine; it also requires more frequent use. It is not usually applied.

The use of sucralfate may be valuable, especially in dogs.

Sucralfate (0.5-1 g every 6 – 12 hours) is an aluminum salt of sucrose sulphate with a covering effect on the gastric mucosa. In an acidic environment (pH <4), it is converted to viscous, dense polymer, which adheres to epithelial cells and the bottom of the ulcer, inhibits pepsin-dependent hydrolysis of the mucosal structural proteins (4).

With long-term use of aluminum compounds there is a risk of poisoning due to the accumulation of aluminum in the organism, although this is rare in animals. Progressive decrease in MCV and microcy-

tosis are early indicators of overdose of aluminum compounds and intoxication (5,6,7).

/The author also notes that the same laboratory abnormalities occur in the case of iron deficiency in patients receiving darbo- or erythropoietin and the interpretation of the test results must be directly related to the clinical condition of the patient and the currently used treatment. /

Symptoms of poisoning are dysfunctions of the nervous and neuromuscular systems, including limb paralysis, decreased response to stimuli, and disturbances in consciousness. Aluminum neurotoxicity depends on its potential for causing chronic inflammation and oxidative stress, which can lead to and / or promote the development of neurodegenerative diseases (8).

Photo 1.

Vomiting, intestinal atony

Gastrointestinal complications (gastroenteritis, intestinal inflammation, anorexia, nausea, vomiting, diarrhea) are very common in animals with advanced uremia (ERDS, AKI V). Despite this, there are not many studies assessing the impact of kidney disease on the functioning of the digestive tract in dogs and cats, most of the research comes from human medicine or from research on rats.

Two potential causes have been described, leading to impaired gastrointestinal function. The first hypothesis assumes that reduced kidney catabolism of gastrin and a reduced number of its inhibitors cause hypergastrinemia, leading to increased secretion of stomach acids (13). Such abnormalities have been demonstrated in 60% of CKD cats in whom hypergastrinemia was linearly associated with the severity of renal disease (14).

The second potential pathomechanism is associated with increased gastric mucosal permeability and "backward diffusion" of hydrochloric acid and pepsin, which leads to the inflammation and release of histamine, further enhancing the secretion of acids (15).

Symptoms include functional disorders that may potentially be associated with uremic gastropathy: delay in emptying the stomach from solid foods (but not fluids) has been demonstrated in rats (16) with CKD, whereas in humans there was reduced myoelectrical activity of the intestinal smooth muscle (17).

Diarrhoea resulting from intestinal inflammation, often hemorrhagic, develops mainly in dogs but is less common than uremic gastropathy. It has been proven that dogs in gastrointestinal disorders include slower gastric emptying, accelerated passage in the small intestine and increased intestinal pH. (18). In cats, the more common problem is constipation, which is usually the result of dehydration and / or use of phosphorus scavengers/ wymiataczy fosforu.

In humans and rodents, the impairment of glucose, fat, magnesium, calcium and folic acid reabsorption was also reported (13).

Parallel struggle with inflammation and reduction of uremia are crucial in the treatment of patients with uremic gastropathy.

The drug particularly recommended in such states is maropitant – a highly selective antagonist of the NK1 neurokinin receptor. Acting at the level of the emetic center, it effectively inhibits vomiting and reduces nausea. It works most efficiently with intravenous supply (administered slowly). When applied orally, it may irritate the gastrointestinal mucosa, therefore it should not be used on empty stomach (9).

Standard dosage: 1 mg/kg sc/iv or 8 mg/kg p.o. every 24 hours.

Ondansetron – s a specific 5-HT3 receptor antagonist – serotoninergic, is characterized by the strongest antiemetic effect in dogs. Recommended dose range: 0.5 mg/kg - up to 1 mg/kg iv (10).

Despite the higher efficacy of ondansetron against vomiting in dogs, maropitant has a certain advantage - it has analgesic effects on visceral pain, both in dogs and cats (11, 12). For this reason, it is usually the first-choice medicine.

A good option for patients with uremic atony of the intestines may be the use of cisapride – a 5-HT4-serotoninergic receptor agonist characterized by peripheral gastroprocessic effect. Dosing: 0.5-1 mg/kg p.o. every 8-12 hours (9).

The co-administration of cisapride with cimetidine should be avoided (this does not apply to other H2 blockers) as it may lead to increased levels of cisapride in blood (13).

Metoclopramide (0.2-0.5 mg/kg every 8 hours), a dopamine receptor antagonist, is more effective as an antiemetic than gastroprokinetic. Contraindicated in cases of suspected bleeding into the gastrointestinal tract, ulceration, perforation, as well as in patients with epilepsy (13).

Decreased appetite and anorexia

Patients with advanced kidney disease, despite the preservation of appetite, often eat too little to cover their daily energy needs. For this reason, it is advisable to use drugs that improve appetite, but only after making sure that the underlying cause of insufficient food intake is not nausea.

Currently recommended drugs are mirtazapine and cyproheptadine in cats and mirtazapine in dogs. Mirtazapine (0.5 mg/kg every 24 hours in dogs, 3.75 mg/cat 1 x every 72 hours) additionally has antidepressant and slight painkiller effect in dogs, it also acts prokinetically on the gastrointestinal tract in healthy animals (19). In contrast, cyproheptadine is used in this species as an antipruritic agent, in cats (1-4 mg/cat every 24 hours) it is used as an appetite stimulant (20, 21).

The author's own experience shows that the tolerance of mirtazepine and cyproheptadine in animals, especially in cats, varies. Due to central effects, sedation or agitation may occur. Cats are very reluctant to take both medicines, often profuse drooling is observed.

One of the most interesting options is capromorelin. It is a direct analogue of the hunger hormone (ghrelin) which causes increased food intake, increased secretion of somatotropin and, as a consequence,

increased muscle mass. It is highly recommended in cachexia and geriatric patients. The dosage in dogs is 3 mg/kg 1 x day, according to the manufacturer, the dose for cats is 2 mg/kg, although according to current information, it may not be sufficient and the dosage should be modified based on the therapeutic effect (23).

Antibiotic therapy

Often patients with uremia require the introduction of antibiotic therapy. One of the reasons is overgrowth of the intestinal flora. Another common problem is the terrible condition of the mouth and teeth. If for various reasons it is not possible to perform a sanitation procedure, antibiotics should be included obligatorily. Similarly, in the case of accompanying infections (e.g. urinary tract or respiratory tract).

The decision to choose an antibiotic should be well-thought and dependent on the target organ and the pharmacokinetics of the chosen substance.

The table below presents selected, most commonly used antibiotics along with the proposed dose reduction in advanced renal failure.

The material listed below is based on medical publications, relatively few studies have been carried out for dogs and cats (3).

Treatment of pain

Patients in exacerbation of chronic renal failure may experience significant discomfort and pain due to the accumulation of uremic toxins, the development of metabolic acidosis and hypertension. In people, headaches and stomach pains are common (especially in mucosal ulcerations). Moreover, most of the animals with end-stage renal function are geriatric patients who, for example, suffer from osteoarthritis of the joints and spine.

The introduction of analgesic therapy should be an inherent element of comprehensive treatment.

- **Non-steroidal anti-inflammatory drugs (NSAIDs)**

  In ESRD, NSAIDs are absolutely contraindicated. Their direct, nephrotoxic action is related to the inhibition of the formation of prostaglandins that condition the extension of the arteriole that supplies blood to the glomerulus. There is a decrease in GFR, sodium and water retention and an increase in blood pressure.

  The use of NSAIDs in combination with inhibitors of the renin-angiotensin-aldosterone system (ARB, iACE) is particularly dangerous because this combination results in a significant reduction in the glomerular filtration rate.

  Side effects of non-steroidal anti-inflammatory drugs in advanced renal disease include significant, acute kidney injury, nephrotic syndrome with interstitial inflammation, renal papillary necrosis, decrease in potassium excretion and thus hyperkalemia, reduction of sodium excretion with fluid accumulation, increased blood pressure and therefore instability of circulatory system. The use of these drugs impairs the treatment of hypertension and increases the nephrotoxicity of iACE and ARB.

  One-off use of drugs from this group can be safe for well-hydrated patients with fairly good renal function and with a fully efficient cardiovascular system, without hypertension and additional metabolic diseases. High doses and long-term use of this group of drugs are unacceptable (3.24)

- **Metamizole** (10-50 mg / kg; do not use on cats).

  The mechanism of action of this drug is not fully understood. It belongs to the group of non-opioid analgesics and is a derivative of pyrazolone. It has been experimentally shown that it does not inhibit cyclooxygenases as strongly as classical anti-inflammatory drugs and is much better tolerated by kidneys (it mainly works by inhibiting central COX-3) (25). In contrast, the typical side effect of pyrazolone derivatives reported in humans is the state of agranulocytosis and a significant decrease in immunity (26).

  Whereas in dogs, metamizole only after a few days of use leads to a decrease in RBC and thrombocytosis and a relatively small decrease in the number of neutrophils (27).

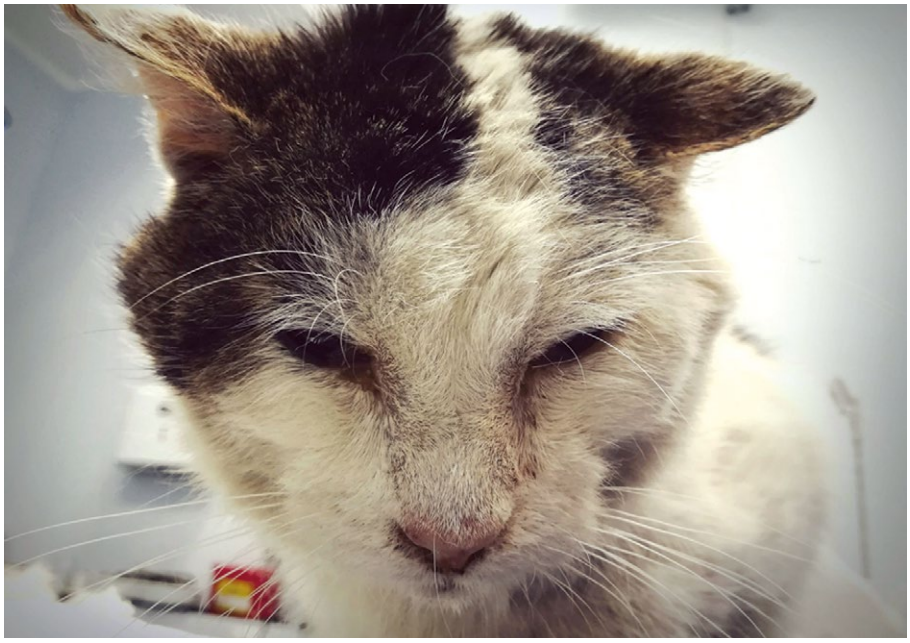

Photo 2.

Table 1.

Chemotherapeutic	Dosage	CKD stage 1-2	CKD stage 3	CKD stage 4
Amoxicillin	12.5-20 mg/kg orally	2-3 x dz	2 x dz	1 x dz
Ampicillin	10-20 mg/kg orally	3-4 x day	3-2 x day	2-1 x day
Ampicillin/sulbactam	10-20 mg/kg orally	3 x day	2 x day	1 x day
Cefalexin	10-25 mg/kg orally	2-3 x day	2 x day	2-1 x day
Ciprofloxacin	10-20 mg/kg orally	100%	75%	50%
Doxycycline	5-10 mg/kg	1-2 x day	unchanged	unchanged
Enrofloxacin	5 mg/kg	100%	25-50%	50-75%
Marbofloxacin	2.75-5.5 mg/kg	100%	75%	50%
Meropenem	8 mg/kg	100%	50% 2 x day	50% 1 x day
Clindamycin	5-25 mg/kg orally in the divided dose	unchanged	unchanged	unchanged

(34,35)

- **Opioids**
  With opioid drugs, we have a choice of a whole group of drugs with painkillers of different potential. Their use, however, is not unpunished. Too high doses will cause respiratory depression and thus interfere with the process of respiratory compensation in patients with metabolic acidosis (29). They show hypotensive effect (lowering blood pressure), which may result in renal ischemia, urinary retention, hyperkalemia. When used chronically, they cause severe constipation. In themselves, however, they do not show direct nephrotoxicity, but some of their metabolites are excreted in the urine and for this reason not all can be used in kidney dysfunction.

  I. **Tramadol** (2-5 mg/kg 2 x dz) – a synthetic agonist of μ, δ and κ receptors, also demonstrates antitussive activity. It inhibits the reversible uptake of norepinephrine and serotonin in the synapses of the descending pain conduction system in the spinal cord. Used in mild to moderate pain. It is known that it does not have a direct nephrotoxic effect. Unfortunately, its metabolites accumulate in the advanced stages of the disease. Moreover, some animals tolerate this medicine poorly, some being drowsy, others may experience paradoxical stimulation (especially in cats) (30.34).

  The drug may cause nausea and dizziness. Low dose protocols are recommended. Excreted by the kidneys by about 30%. Considered to be safe.

  The use of tramadol with an extended period of action (retard form) is not recommended (3).

  II. **Buprenorphine** (20 μg/kg every 6-8 h) - semi-synthetic derivative of thebaine, the alkaloid of opium. It is a partial agonist of the μ and δ opioid receptors and the κ receptor antagonist. Well soluble in fats, in 96% is bound to plasma proteins. It is characterized by low bioavailability after oral administration, due to inactivation in the intestine, applied intramuscularly, subcutaneously and on mucous membranes. Buprenorphine on its own does not cause respiratory depression or sedation effect, but its metabolites cause it (31). Metabolized in the liver to, inter alia, norbuprenorphine, which also demonstrates a weak analgesic effect. According to recent information, neither buprenorphine nor its metabolites are excreted via the kidneys, so the drug is considered safe even in advanced disease and does not require dose reduction, yet should be used with caution for the reasons mentioned earlier. Usually well tolerated by dogs and cats. Effective in combating moderate pain. The effect develops approximately 20-40 minutes after administration (34).

  III. **Methadone** (dogs: 0.1-0.5 mg/kg, 0.1 mg/kg iv, cats: 0.1-0.3 mg/kg) - a synthetic agonist of μ opioid receptors, metabolized in the liver, excreted by gastrointestinal tract and kidneys to a similar extent. It has been proven (in humans) that in the case of kidney failure there is an increased excretion of metabolites of methadone through the digestive tract, therefore it does not accumulate in patients with renal dysfunction.

  There is no data on whether a similar mechanism works in animals. Considered low risk even in advanced kidney disease, it does not require dose reduction, but should be used with caution. Narcotic medication, used in the treatment of moderate to severe pain (32).

  IV. **Fentanyl**, Fentanyl, hydrocodone and hydromorphone – can be used in patients with kidney failure.

  V. **Morphine and codeine** are contraindicated; if necessary, the starting dose should be reduced up to 50-75% of the starting dose depending on the degree of GFR (33).

- **Other medications**

  I. **Gabapentin** – an anticonvulsant drug structurally similar to γ-aminobutyric acid (GABA), with proven analgesic properties against neuropathogenic pain. Practically, it does not undergo any biotrans-

Photo 3.

Table 2.

Systolic blood pressure	Diastolic blood pressure	Risk of organ damage	Stage of hypertension	
< 150	< 95	minimum	AP0	normotensy
150-159	95-99	small	AP1	sub-clinical hypertension
160-179	100-119	moderate	AP2	hypertension
> 180	< 120	high	AP3	severe hypertension

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Note: in Greyhounds, the blood pressure is higher by 20 mmHg

Table 3.

Classification	Medicine	Dosage	COMMENTS
ACEi	Benazepril	Dogs: 0.25-0.5 mg/kg every 24 h Cats: 0.5-1 mg/kg every 24 h	In ESRD dose reduction by 50-75%
	Enalapril	Dogs: 0.25 - 1,0 mg/kg every 24 h Cats: 0.25 mg/kg every 24 h	Excreted mainly via the kidneys, not recommended
	Ramipril	0.125 mg/kg every 24 h	In ESRD dose reduction by 50-75%
	Imidapril	0.25 mg/kg every 24 h	In ESRD dose reduction by 50-75%
ARBs	Telmisartan	1 mg/kg	In ESRD dose reduction by 50-75%
Calcium channel blockers	Amlodipine	Dogs: 0.1–0.2 mg/kg every 24h to 0.5 mg/kg every 24h Cats ≤6 kg: 0.625 mg/cat every 24h Cats >6 kg: 1.25 mg/cat every 24h	Well tolerated in kidney diseases. It has been experimentally shown that kidney disease does not significantly affect the pharmacokinetics of the drug.
Beta-blockers	Atenolol	Dogs: 0.25-1.0 mg/kg every 12 h Cats: 6.25-12.5 mg/cat every 12 h	In ESRD dose reduction by 50-75% They can lower the blood pressure not only by lowering the heart rate and stroke volume, but also by inhibiting the release of renin. Often ineffective in cats. In dogs, the effect depends on the cause of hypertension (36.37). The decision to introduce / modify the dosage of the drug depends on the cardiological evaluation!
Aldosterone antagonists	Spironolactone	1.0-2.0 mg/kg q 12-24 h	To be withdrawn in ESRD.
Alpha-blockers	Prazosin	Dogs: 0.5-2 mg/kg q 8-12 h Cats: 0.25-0.5 mg/cat q 24 h	The use of α1-blockers leads to peripheral vasodilation without affecting cardiac contractility. Incorporated when the use of ACEi and CCB does not bring the expected reduction in overpressure. Possible side effects include hypotension, vomiting, tachycardia, loss of appetite, and incontinence It is recommended to use the lowest possible dose, the risk of accumulation.
	Phenoxybenzamine	Dogs: 0.25 mg/kg every 8-12 h or 0.5 mg/kg every 24 h Cats: 2.5 mg/cat every 8-12 h or 5 mg/cat every 24 h	
Vasodilators	Hydralazine	Dogs: 0.5-2 mg/kg every 12 h Cats: 2.5 mg/cat q 12-24 h	Can be used when the ACEi + CCB combination does not bring the desired effect. To be introduced with caution starting from the lowest doses.
Loop diuretics	Furosemide	1-4 mg/kg every 8-24 h	Do not require dose reduction; It has been experimentally demonstrated that low doses of diuretics can favorably affect ESRD patients, protecting against fluid retention and hyperkalemia. The decision about introducing these drugs should be well considered, as too early including in the therapy can deepen the degree of dehydration and ion problems.
	Torasemide	0.1-0.6 mg/kg every 24 h	

(34, 36, 37, 38, 39, 40)

formation in the body, not binding to plasma proteins either. It can be an alternative to non-steroidal anti-inflammatory drugs in the management of chronic pain in patients with co-existing renal disease. However, since the elimination of the drug occurs mainly in the urine (up to 80%), it is recommended to reduce the doses from 50 to 70% and extend the interval between successive administrations in the advanced stages of the disease. The precise pharmacokinetics of the drug in patients with kidney disease have not been investigated, therefore the use and dosage of gabapentin should be determined individually based on the severity of the disease and the effectiveness of action.

II. **Maropitant** – an antiemetic from the class 1 neurokinin receptor antagonist. It blocks the transmission of the signal mediated by the substance P and exerts an analgesic effect. It is effective against visceral pain.

Hypertension and proteinuria

Topic discussed only in selected aspects, only for patients with ESRD. Detailed description of the issue, as well as discussion of treatment regimes for hypertension, would require separate publication.

Most patients with kidney failure develop hypertension, which is a consequence of the activation of the renin-angiotensin-aldosterone system and secondary to this, of sodium and water retention. In addition, nephrogenic hyperactivity of the parathyroid glands results in an increase in intracellular calcium concentration, which leads to vasoconstriction and further increase in blood pressure. Moreover, the impairment of the systems' actions responsible for vasodilatation (reduced synthesis of nitric oxide, a deficiency of cofactors for its production) intensifies this condition. The

Table 4.

	Dosage	Frequency	Comments
darbopoetin	1 mcg/kg	1 x week	The increase in the number of hypochromatic erythrocytes and the low level of hemoglobin may indicate iron deficiency.
erythropietin beta	100 U/kg	every 3 days	
iron dextran	dogs: 10-20 mg/kg cats: max. 50 mg/cat	1-2 x a month	administered deeply intramuscularly; the risk of shock with supply of iv

(34, 42, 43)

mechanism of developing hypertension in kidney diseases is quite complicated and, what's more, it does not occur in every case.

Improper management of kidney failure patients (fluid overload, incorrect selection of fluids, use of erythropoietin or darbopoetin without monitoring of blood pressure) causes the deterioration of existing hypertension or may reveal subclinical hypertension.

In veterinary medicine, the main treatment for hypertension is the use of angiotensin-converting enzyme inhibitors (ACEi), angiotensin receptor blockers (ARBs) and calcium channel blockers.

ACEi and ARB drugs reduce the pressure relatively little, usually about 10-15%, and are used mainly for the treatment of proteinuria. They also demonstrate cardio- and nephroprotective effects, but lowering the filtration pressure may cause an increase in creatinine. The acceptable increase is up to 30% of the initial value while maintaining the well-being of the animal.

In the ESRD conditions, these drugs require absolute dose reduction and sometimes even withdrawal, even at the cost of increasing the degree of proteinuria. The purpose of this procedure is to maintain the residual renal function and to improve the degree of filtration.

Amlodipine is the drug of first choice in cats, it has also been shown to affect the reduction of proteinuria in this species.

In dogs, the first-choice drug is ACEi / ARB, but sometimes there is a need to use several different drugs from different groups.

Loop diuretics are unlikely to be of much use for the treatment of hypertension in animals but may be useful in animals with hypertension and oliguria leading to overhydration.

The table below presents the selected drugs with doses and comments on their use in patients with ESRD.

The author points out the fact that blood pressure disorders may also be a consequence of endocrine and cardiac diseases. The decision to initiate treatment of hypertension should be made after excluding other potential causes.

Treatment of anemia

In patients with ESRD, the benefits of blood transfusion should be considered in combination with the use of bone marrow stimulation. In the case of end-stage patients, stimulation may not bring the expected effects due to the time required to achieve hematopoiesis. Nevertheless, chronic patients tolerate mild anemia quite well and are able to feel well despite the RBC deficit. Implementation of stimulation is almost always associated with deterioration of the degree of hypertension, so both the necessity and the choice of the method should be selected individually for each patient, his physiological condition and current needs.

The use of both darbo- and erythropyntine requires the simultaneous supplementation of iron, B vitamins and often folic acid.

Fluid therapy

In patients with ESRD, fluid therapy must be used with extreme caution because of the risk of overhydration. The selection of fluids must be based on the individual needs of each patient. Currently, the use of saline is not recommended as the increase in sodium concentration increases metabolic acidosis and the degree of hypertension. It is also important to consider loop-based diuretics unless there is hypokalemia. The author's own experience shows that the more frequent use of less amounts of liquids is better than the periodic supply of more. Such procedures ensure better control of hydration, reduce the risk of patient overhydration, and longer maintain the well-being of animals undergoing treatment.

Sometimes animals, despite seemingly fatal results, are able to maintain the end stage of the kidneys and function normally, displaying all the behavior characteristic of their species. It should be emphasized, however, that achieving such effects requires a lot of commitment and accuracy from the owner.

Only selected drugs are shown in the material.

It should be remembered that the treatment covers the whole animal and not only clinical symptoms and abnormalities in laboratory tests.

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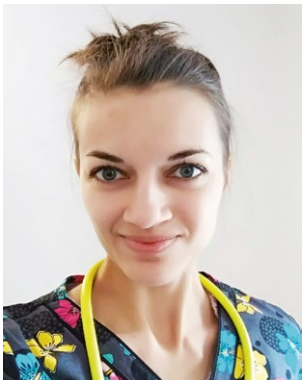
Nodular dermatofibrosis and renal cystadenocarcinoma in German pointer – CASE DESCRIPTION



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Summary

The article describes the case of nodular dermatofibrosis and renal cystadenocarcinoma in the German pointer. Initially, this phenomenon was regarded to be characteristic only for German shepherds. Over time, case reports were published describing similar or identical changes in representatives of other breeds and crossbreeds. The described disease syndrome in German Shepherds is an inherited autosomal dominant. It is an incurable disease, and therapeutic treatment is limited only to the relief of symptoms. In the described bitch, proliferative lesions within the skin appeared in the first months of life. The changes in the kidneys were only shown in the ultrasound examination at the age of 11 years. At the age of 15, the bitch was euthanized.

A case report

The description concerns a 12-year-old, neutered German short-haired pointer bitch with a roan-like coat. Jona was referred for a nephrology consultation in April 2014 due to suspected kidney abscesses. The anamnesis showed that the first ultrasound examination of the bitch was at the age of 11 (January 2014). The kidneys were then normal in size, about 6.5 x 3.7 cm, in the right kidney a cyst with a diameter of about 1.3 cm was shown, thin-walled, aechogenic, with a single wall partition about 1.7 mm, regular. The surrounding flesh was unchanged, the cortico-spinal differentiation was preserved. There were no visible deposits and no stagnation.

Ureter, urinary bladder and urethra were defined as without any obvious changes. A year later (March 2015), the kidneys showed already advanced structural changes in the ultrasound examination. In the cranial pole of the left kidney there was a focal lesion with a diameter of 10.3 cm, thick-walled, with the presence of a concentrated fluid, with the accumulation of the cellular component.

Between the cortex layer and the described lesion, a hyperechoic area of 2.6 x 2.1 cm was visible, around which the accumulation of free fluid was visible. The pathological vascularization of the described lesion and infiltrative features were not shown. Ultrasound examination indicated the presence of purulent cystic lesion. The left kidney pelvis was extended to approx. 0.7 cm, while the initial ureteral section widened to approximately 0.5 cm. The left kidney corticospinal system had covering features. In the right kidney, a cystoid-shaped, thin-walled lesion with a diameter of approx. 7.5 cm, filled with a clear liquid was depicted. The pelvis was slightly widened (up to approx. 0.3 cm). In the blood test, no significant changes were found (Table 1). The patient's urine, which was collected during natural micturition (Table 2), was also examined.

At the same time, echocardiography was performed, in which the changes associated with mitral regurgitation in the autocompensated phase, without indications for therapy, were demonstrated.

A matter seemingly unrelated to the current state of Jona was the occurrence of subcutaneous nodules all over the body. Ac-

Photo 1.
Jona

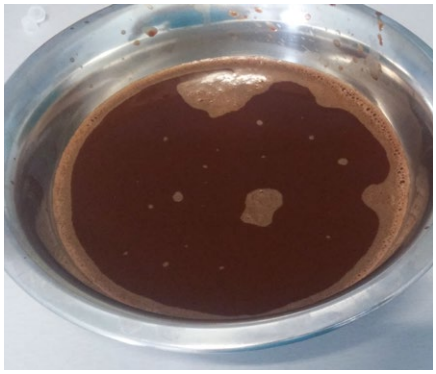

Photo 2.
Fluid from the right kidney cyst puncture

cording to the owner, they have appeared since the first months of the bitch's life. In 2014, during the visit to the oncologist, numerous hard skin lesions were described on the whole skin surface, mainly on the head and ears, with a diameter of 3 to 8 mm. The result of thin needle biopsy showed subcutaneous adipose tissue inflammation, with granuloma hyperplasia features.

Differential diagnosis should include well-differentiated sarcoma (unlikely) and nodular dermofibrosis. Two years later, some changes on the forelimbs of Jona and bacterial infection occurred. Antibiotic therapy was included, followed by health improvement.

In April, Jona was brought to her GP with symptoms of severe weakness, tucked up, painful stomach and vomiting. After the ultrasound examination, there was a suspicion of a right kidney abscess and peritoneal inflammation. Right-sided nephrectomy was considered, while due to the simultaneous strong remodeling of the left kidney, an attempt at pharmacological treatment was made. At this time, renal parameters were slightly increased: creatinine was 2.0 mg / dl, and urea 51 mg / dl. A test was also carried out for Lyme disease, anaplasmosis, erlichiosis and dirofilariosis. A negative result was obtained. The presence of parasites from Babesia type was also excluded. In the urinalysis, apart from the reduced specific gravity, no abnormalities were observed.

The following treatments were implemented: intravenous fluid therapy, ranitidine, maropitant and ceftriaxone intravenously. After one week of treatment, oral antibiotics were continued with cefuroxime for the next 3 weeks. The patient's condition improved significantly from day to day. After one week of therapy, the renal parameters were already within the reference values.

After stabilization of the general condition, the patient was brought to a nephrological consultation. During the visit, Jona's body weight was 24 kilograms, the body mass index was 5 (on a 9-point scale), and hydration was normal. Behind the ribs, on the right side there was a large, hard, painless formation. The patient's body temperature was 37.7°C, and the blood pressure measured by an apparatus using the oscillometric method was about 130/100. Auscultated heart and lungs remained unchanged. Vulva was clean. The ultrasound image of the kidneys was unchanged compared to the one described earlier. Under ultrasound guidance, puncture of the right kidney cyst was performed. The fluid was sent for microbiological and cytopathological examination. Macroscopically, the liquid was yellow-

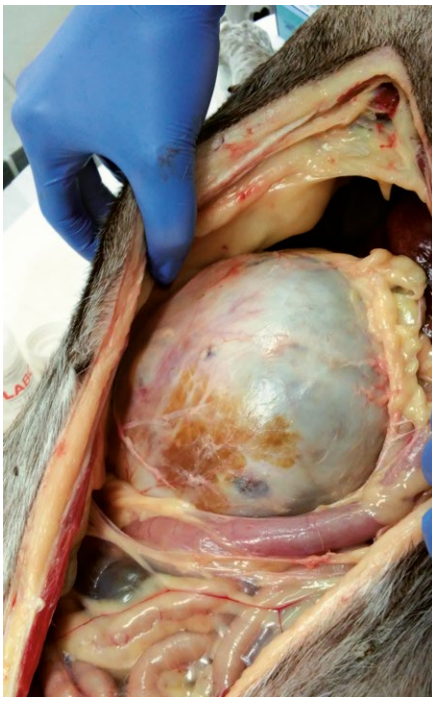

Photo 3.
Abdominal section: right kidney

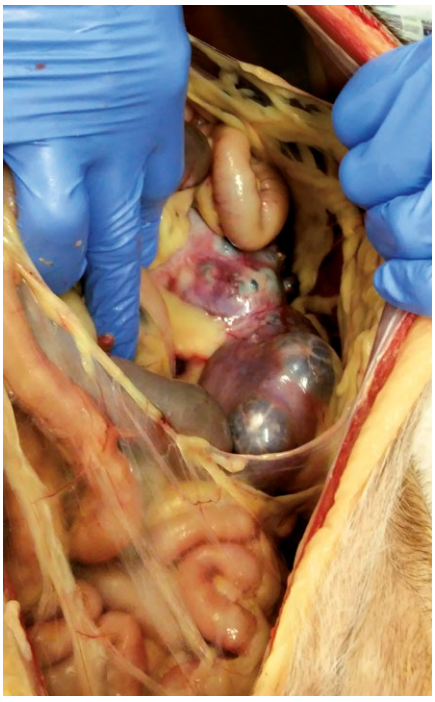

Photo 4.
Abdominal section: left kidney

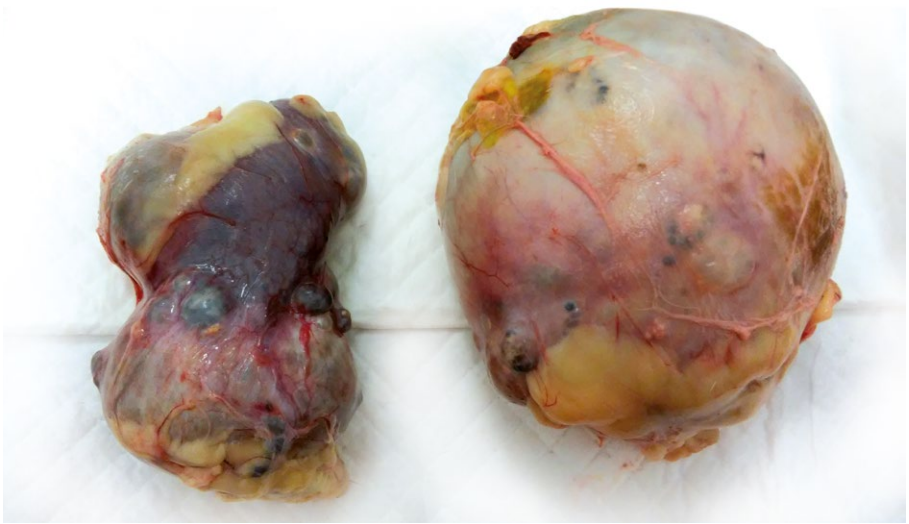

Photo 5.
Post-mortem left and right kidney

brown in color (Figure 1). The result of the examination of the contents of the right kidney cyst was as follows:

Diagnosis: low-cell smears, with the presence of a very large number of erythrocytes, including leached ones, single neutrophils, eosinophils, macrophages loaded with hemosiderin, lymphocytes were noted. In the smears obtained from the transferred fluid after centrifugation, very many leached erythrocytes were found.

Comment: Due to the small number of cells to be evaluated, a cytological diagnosis is impossible. However, the absence of abnormal cells may suggest the presence of a kidney cyst. Due to the presence of very numerous erythrocytes and single macrophages loaded with hemosiderin in the differential diagnosis, the presence of hematoma should be considered.

The microbiological examination did not show the presence of bacteria.

During the visits, urine was also collected using the cystocenthesis method and sent for bacteriological examination. The culture turned negative.

Since the first nephrological consultation, the bitch has felt very well for over a year. The right kidney did not undergo any visible ultrasonographically structural changes, while the content of the cyst changed its consistency. There were focal compaction and inclusions forming partitions. The left kidney has been remodeled during the year. The shape began to resemble the heart, cysts increased and new ones appeared. The renal parameters remained normal all the time. Urine tests showed only reduced urine specific gravity. No other irregularities were noticed.

During the follow-up visit in July 2017 (one year and three months after the first visit to the nephrologist) the diameter of the right kidney cyst was about 15 cm. Vomits appeared in the bitch and there was a suspicion of cysts pressure put on the stomach. A cystic puncture was performed and approximately 600 ml of the yellow-brown liquid was drained. Laboratory fluid was sent again. The same result was obtained as last year. After three months, another puncture was necessary. About 1200 ml of fluid was drained.

From April 2017, the patient began to suffer from joint pain associated with degenerative changes. Jona began to take extemporaneous anti-inflammatory drugs, mainly firocoxib. After the opioid drugs, no improvement was observed. Rehabilitation procedures were also started. From April 2017, the kidney parameters began to gradually increase (Table No. 3). In May, 1500 ml of fluid was drained from the right kidney cyst. In the ultrasound image no normal kidney parenchyma was visible, only the thick-walled capsule remained.

In June 2017, Jona began to give bloody urine. A urine sample was sent for general examination (Table No. 6) and microbiological examination. An antibiotic and symptomatic treatment were included. Despite the therapy, there was no improvement. Jona felt worse day by day. Due to poor general condition and poor prognosis, euthanasia was decided. Post-mortem fragments were taken for histopathological examination. Here is the result:

In the examined areas of all the resected kidneys it was found that multicuspid, moderately cellular, non-obstructed and infiltrating epithelial tumour located in the cortex, the core, and in some sections also penetrating into the pelvis. The tumour cells were polygonal and arranged in the structures of the nature of wires, with papillary projections directed to the light, lined with one layer or several layers of cancer cells. These neoplastic cells had a weakly marked cytoplasmic limb, a small amount of eosinophilic and slightly spiked cytoplasm, and one round oval nucleus with slightly mottled chromatin and one eosinophilic nucleus. Anizocytosis and anisocariasis were in-

Table 1. Results of morphological and biochemical tests of blood taken in February 2015.

The tested parameter	The result obtained	Reference values
Erythrocytes	6.5	5.5 – 8.5 T/l
Hematocrit	44.5	37.0 – 55.0 %
Leukocytes	5.3	6.0 – 12.0 G/l
Creatinine	1.2	0.5 – 1.7 mg/dl
Urea	44.9	20.0 – 50.0 mg/dl
T4	2.13	1.5 – 4.0 ug/dl

Table 2. Urine test results from February 2015.

The tested parameter	The result obtained	Reference values
Specific weight	1.02	1.016 – 1.045
pH	6.5	< 6.5
Leukocytes	0-2 in the high power field	Single in the preparation
Erythrocytes	0-2 in the high power field	Single in the preparation
Bacterial flora	Mediocre	Mediocre
Epithelia	Single Polygonal in the high power field	Single
Casts	Not found	Single
Crystals	Not found	None
Protein / creatinine ratio	0.07	< 0.6

Table 3. Blood test results from the end of April 2017.

The tested parameter	The result obtained	Reference values
Erythrocytes	6	5.5 – 8.5 T/l
Hematokrit	35.8	37.0 – 55.0 %
Leukocytes	12.29	6.0 – 12.0 G/l
Neutrophils	11.2	2.9 – 13.6 G/l
Lymphocytes	0.63	1.1 – 5.3 G/l
Monocytes	0.34	0.4 – 1.6 G/l
Eosinophils	0.1	0.1 – 3.1 G/l
Creatinine	2.2	0.5 – 1.7 mg/dl
Urea	83	20.0 – 50.0 mg/dl
Total protein	6.1	5.5 – 7.5 g/dl
Albumins	3.6	3.3 – 5.6 g/dl
Sodium	321	320 – 360 mg/dl
Potassium	24.8	16.0- 21.0 mg/dl
Calcium	10.8	8.4 – 11.5 mg/dl
Phosphorus	5.9	2.5 – 6.3 mg/dl

Table 4. Urine test results at the end of April 2017.

The tested parameter	The result obtained	Reference values
Specific weight	1.015	1.016 – 1.045
pH	7.0	< 6.5
Leukocytes	0-2 in the high power field	Single in the preparation
Erythrocytes	0-2 in the high power field	Single in the preparation
Bacterial flora	Mediocre	Mediocre
Epithelia	Single polygonal in the high power field	Single
Casts	Not found	Single
Crystals	Not found	None
Protein / creatinine ratio	0.21	< 0.6

Table 5. Blood test results from 08.06.2017

The tested parameter	The result obtained	Reference values
Erythrocytes	5.0	5.5 – 8.5 T/l
Hematokrit	30.2	37.0 – 55.0 %
Platelets	298	150 – 500 G/l
Leukocytes	5.42	6.0 – 12.0 G/l
Creatinine	2.7	0.5 – 1.7 mg/dl
Urea	169	20.0 – 50.0 mg/dl
Total protein	6.6	5.5 – 7.5 g/dl
Sodium	318	320 – 360 mg/dl
Potassium	20.2	16.0- 21.0 mg/dl
Calcium	11.5	9.2 – 12.0 mg/dl
Phosphorus	7.5	2.2 – 5.0 mg/dl

Table 6. Blood test results from 13.06. 2017 r.

The tested parameter	The result obtained	Reference values
Specific weight	1.015	1.016 – 1.045
pH	5.5	< 6.5
Leukocytes	3-5 in high power field	Single in the preparation
Erythrocytes	Fresh and leached with a thick layer per high power field	Single in the preparation
Bacterial flora	Numerous	Mediocre
Epithelia	Single polygonal in the high power field	Single
Casts	Not found	Single
Crystals	Not found	None

significant and the mitotic index was low. In many places, some tubular structures were significantly widened and formed cystic structures (with a size of 0.4 to 1.4 cm), filled with a bright, acid-absorbing material or were empty. In some places, strong fibrosis around the tumor was visible (reactive desmoplastic reaction). Cancer cells were also found in the lymph vessels.

Diagnosis: kidney cancer, with features of renal cystadenocarcinoma.

Discussion

The simultaneous occurrence of nodular dermatofirosis, cystadenoma or cystadenocarcinoma and sometimes leiomyomas of the uterus has been quite accurately described in German shepherds. This syndrome established a form of autosomal dominant inheritance [2,3,6,7,8]. In time, similar cases were also reported in representatives of other breeds such as: golden retriever [5], boxer [1], labrador retrivers, Scottish setter (gordon) and crossbreeds of unknown origin [1].

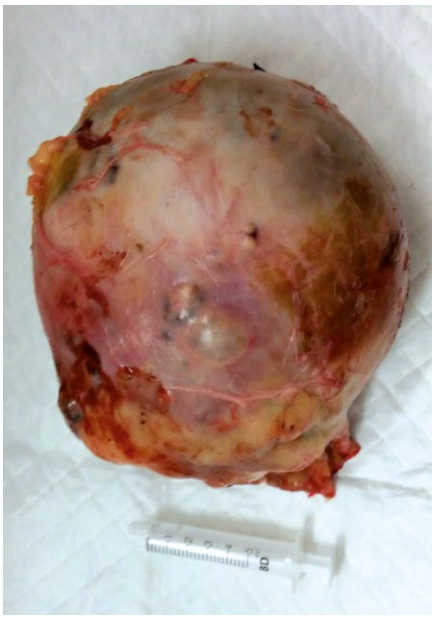

Photo 6.
Post mortem: right kidney

Pathogenesis has not been known so far. There are three theories that try to explain the occurrence of this phenomenon.

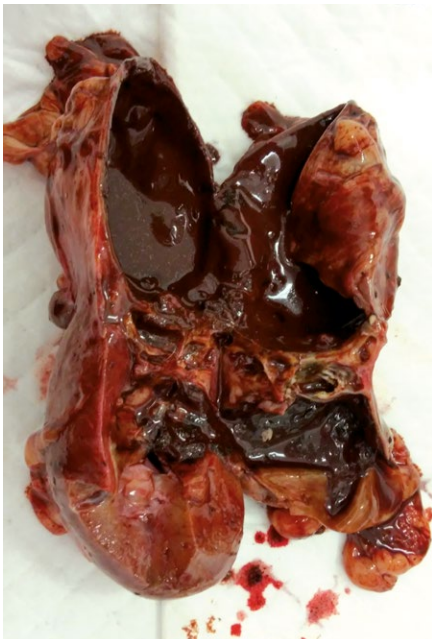

Photo 7.
Left kidney: longitudinal section

One hypothesis assumes that nodular dermofibrosis is a paraneoplastic syndrome secondary to neoplastic renal remodeling. According to the second theory, these are two different diseases that appear independently of each other, and it is only the mechanism of inheritance that connects them [2,3,5]. The third hypothesis assumes the simultaneous initiation of fibrosis within the skin and kidneys. Over time, the tubules become obstructed and, as a consequence,

cysts develop. In dogs with a genetic tendency, there are tumor lesions [1].

Due to the predictable course of the disease, the prognosis is cautious. The patient's life expectancy depends on the progress of kidney disease, on the presence of infiltrates or cancer metastases (sternal and abdominal lymph nodes, lungs, liver) and on the degree of discomfort associated with the presence of nodules. Analyzing the described cases, the time between making a diagnosis and death ranged from 3 months to 5 years. Some of the dogs described have been euthanized for reasons beyond the described disease [1,2,3,4,5].

Summary

Nodular dermofibrosis with simultaneous kidney disease associated with the formation of cysts can probably be found in dogs of all breeds and hybrids. In every patient diagnosed with nodular dermofibrosis, periodic ultrasound should be performed to monitor the possible development of the kidney diseases described above. Therapeutic treatment is based only on the reduction and alleviation of emerging clinical symptoms. In the case of unilateral remodeling of the cystic kidney, nephrectomy is indicated. Unfortunately, changes generally occur on both sides. Bitches should be ovariohysterectomised and males excluded from reproduction [9].

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The efficacy of Renal Dog and Renal Cat and the RenalVet in dogs and cats with chronic renal failure

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Chronic kidney disease (CKD or CRF, chronic renal failure) is a disorder often noted in pets. In its course, the function of any part of the kidney may be impaired, such as glomerulonephritis, renal tubules, interstitial tissue or renal vessels. The disease is generally manifested by structural changes in the kidneys and disorder of their function, the effect of which is the accumulation of uremic toxins in the body and disturbance of the homeostasis of the body. Chronic renal failure is an irreversible and progressive condition, even if the primary cause leading to its development has been eliminated. Clinical symptoms accompanying the disease depend on the type and severity of kidney damage (3.5). According to the guidelines of the International Renal Interest Society (IRIS), there are four stages of chronic renal failure. Their classification is presented in Table 1 (2).

The diagnosis of CKD is based on the analysis of the results of the clinical examination, serum creatinine (sCr) and urea, the assessment of urine compacting capacity, and the demonstration of proteinuria. sCr is the most frequently used disease marker, however, it is characterized by low sensitivity. It is generally accepted that at least a 75% decrease in glomerular filtration is necessary to increase serum creatinine. In connection with the above, when the CKD is suspected, the diagnostic approach to the patient must be comprehensive, so that the obtained results do not raise any doubts that we are dealing with this disease, and not, for example, prerenal or post-renal disorders (3, 8).

The purpose of CKD treatment is to stop the progression of the disease, while ensuring a proper quality of life for the patient. Maintenance of the good quality of life can be achieved through the use of appropriate diet in animals, minimizing the consequences of the disease and the identification and control of risk factors that can lead to a sharp worsening of the disease. Therapy should be initiated even if the patient does not have clinical symptoms. There is strong evidence that the use of a "renal diet" contributes to the slowing down of the disease and prevents the occurrence of uremic crisis (4,7). Pharmacological treatment should be adjusted individually to the patient depending on the stage of the disease, the severity of clinical symptoms and the presence of possible complications such as hyperphosphatemia, hypertension, proteinuria, acid-base disorder, anemia, urinary tract infection and dehydration. While all therapeutic goals have been achieved, the patient's quality of life will probably improve, and the disease itself will be slower (3).

The aim of the study was to evaluate the efficacy of Renal Dog® and Renal Cat® (Vetexpert) and RenalVet® dietary supplement (Vetexpert) in dogs and cats with CKD.

Material and methods

The research was conducted from February 2017 to February 2018. It included 20 cats aged 2-19 years and 24 dogs aged 2.5-17 years with chronic renal failure. Age, sex and breed of animals are presented in Tables 2 and 3. Chronic renal failure was diagnosed based on information obtained in the past as well as clinical symptoms (lack of appetite, weight loss, disturbances of urina-

Table 1. Stages of chronic kidney failure

CKD stage	I	II	III	IV
Clinical symptoms	None	Subtle to mild (e.g. PU/PD) or none	May be many clinical extrarenal symptoms	Growing risk of systemic clinical symptoms and uremic crisis
SDMA	Correct to slightly increased	Slightly increased to increased	Increased	Increased
Urea and creatinine concentration	No azotemia	No azotemia to mild azotemia	Azotemia	Azotemia
Protein concentration in urine	No proteinuria	No proteinuria or border proteinuria	Proteinuria	Proteinuria
Specific gravity	Normal	Normal to mildly reduced	Reduced	Reduced
Prognosis	Good	Good to moderate	Moderate to weak	Weak

tion), and determining the concentration of phosphorus, creatinine and urea in serum, determining of urine specific gravity, determination of SDMA concentration and biochemical analysis of urine. On the basis of the obtained results, the degree of chronic renal failure was also classified according to Table 1.

After diagnosing chronic renal failure, all animals were prescribed a medicated feed Renal (Vetexpert) and RenalVet® dietary supplement. In addition, the animals were treated symptomatically, depending on the need. Seven individuals in the group of cats and seven individuals in the group of dogs, whose owners had a problem with administering medicated feed and dietary supplement and gave up their administration (animals showed aversion to the food and supplement) were treated as a control group. In connection with the above, the group of cats consisted of 13 test animals (receiving medicated feed and dietary supplement) and seven control ones ones (fed with standard feed), while a group of dogs consisted of 17 test animals (receiving medicated feed and dietary supplement) and seven controls (fed with standard domestic food).

Three months long controls were performed in all animals, indicating how feeding Renal® and the RenalVet® dietary supplement affects: clinical status, urea, creatinine and serum phosphorus, urine specific gravity, SDMA value and urine protein concentration. Changes in the values of the tested parameters during the own observations are presented in Tables 4-15.

Results of own observations

In the group of tested cats (1-13) receiving medicated feed and dietary supplement the mortality rate was 30.8% (4/13) and was significantly lower than the mortality rate in the control group (14-20), which was 57.1%. (4/7). All fallen animals, both in the treatment and control groups at the time of reporting to the veterinary clinic were in the third or fourth stage of CKD. Three of four cats of the treatment group that died were included in observation for at least 9 months (followed by demise) and one over 6 months. Of the 4 fallen cats of the control group, two survived the period of over 3 months, and the next two 6 months.

In all the other nine cats of the treatment group, the administration of food and dietary supplement caused a delay / detention in the progression of the disease process. In eight individuals, throughout the period of observation, chronic renal failure persisted in stage I-II and in one animal in stage III. (Table 16)

In the control group of all three individuals who survived the observation period, the disease progression from the 1st to 4th stage of CKD (in one individual) and from the 2nd to 4th stage (CKD) were recorded over 12 months (Table 16). Changes in the parameters investigated, based on which the progression of CKD during the own observations were recognized and monitored, are presented in Tables 4-9

In the group of dogs examined (1-17), receiving medicated feed and dietary supplement, the mortality rate was 23.5% (4/17) and was significantly lower than the mortality of animals in the control group (18-24), which was 71.4% (5/7). All animals that died in the treatment group were in the third or fourth stage of the CKD when they were registered at the veterinary clinic. In turn, in the fallen animals in the control group, a rapid progression of the disease process from the second to the fourth phase of CKD was observed.

Three of the four fallen dogs of the treatment group were followed for at least 9 months (followed by falls) and one over 6 months. Of the 5 fallen control dogs, two survived the period of over 9 months, and the next three during 6 months.

It is noteworthy that in all the other 13 dogs of the treatment group, the administration of food and dietary supplement resulted in a delay / detention in the progression of the disease process. In 12 specimens throughout the period of observation, chronic renal failure persisted in the I-II stage, while in one animal the disease process at the end of the observation passed in the third stage (Table 17).

In the group of control animals, in both individuals, who survived the observation period, the disease process from I to IV CKD

Renal Dog 2 kg, 14 kg

Renal cat 2 kg

stage was recorded within 12 months (Table 17). Changes in the tested parameters, on which the progression of CKD was based during the own observations and which were recognized and monitored, are presented in Tables 10-15.

Discussion

In our research, the effectiveness of Renal Dog® and Renal Cat® feeds and the RenalVet® dietary supplement in the prevention of chronic renal failure in dogs and cats was evaluated.

Feeds for animals with chronic renal failure are modified standard feeds, and modifications can be carried out in several ways. It should be remembered that lowering the protein content may not bring satisfactory results. A new feed should be introduced gradually and only if clinical symptoms can be controlled (3,7,8). In our study, a product with a reduced content of phosphorus and protein was used, allowing to reduce the rate of kidney disease, while ensuring optimal digestion and absorption of protein in the gastrointestinal tract. The test feed was enriched with alpha-lipoic acid (supports the neutralization of free radicals formed in the course of kidney diseases) and L-carnitine and fat (they support the burning of fatty acids and energy production from fat as a result of which the body does not use proteins for energy purposes and does not burden the kidneys with its metabolic products).

The effect of the medicated feed was supported by the action of the RenalVet® dietary supplement, which contains calcium carbonate, chitosan and vitamin D. Calcium carbonate in the digestive tract disintegrates, and the calcium ion, released from it, binds to the phosphate in the food, forming insoluble and non-absorbed calcium phosphate. As a result, the amount of phosphorus absorbed from food is reduced.

Chitosan used in combination with calcium carbonate as a preparation supporting calcium binding in the gastrointestinal tract results in a decrease in serum phosphorus concentration, a decrease in the level of parathyroid hormone and a decrease in the excretion of phosphorus in the urine. The use of such a mixture can be regarded as an alternative and support for veterinary diets for dogs and cats with renal insufficiency. Vitamin D contained in the preparation is primarily to be treated as a supplement to potential deficiencies of this compound caused by renal failure.

In our own study, the use of medicated feed together with a dietary supplement over a period of 12 months contributed to the inhibition of disease progression in both cats and dogs treated. The concentration of creatinine, phosphorus, urea and SDMA, urinary protein and urine specific gravity in patients in this group were reasonably stable throughout the observation period. On the other hand, control animals not receiving feed and supplements showed a steady progression of the disease process (Tables 4-15).

Table 2. Cats used in own research

Description of cats with chronic renal failure used in own research				
Nr of animal	**age**	**sex**	**breed**	**procedure**
1	5 years	male	Norwegian Forest Cat	Diet + supplement
2	8 years	male	Russian Blue	Diet + supplement
3	14 years	male	European	Diet + supplement
4	11 years	male	European	Diet + supplement
5	19 years	male	European	Diet + supplement
6	2 years	male	European	Diet + supplement
7	11 years	female	European	Diet + supplement
8	13 years	male	European	Diet + supplement
9	10 years	female	Persian cat	Diet + supplement
10	8 years	male	Brytyjski	Diet + supplement
11	12 years	female	Persian cat	Diet + supplement
12	8 years	male	European	Diet + supplement
13	10 years	male	European	Diet + supplement
14	12 years	female	Perski	Nutritioned with standard feed
15	7 years	male	European	Nutritioned with standard feed
16	8 years	male	European	Nutritioned with standard feed
17	12 years	female	Devon rex	Nutritioned with standard feed
18	14 years	male	European	Nutritioned with standard feed
19	10 years	male	European	Nutritioned with standard feed
20	9 years	female	Siamese	Nutritioned with standard feed

Confirmation of the effectiveness of the implemented procedure, along with the inhibition of the disease process, was the fact of a reduced percentage of deaths in the group of animals receiving food and supplement compared to the control group (in the group of cats 30.8% vs. 57.1%, and in the group of dogs 23.5 % vs. 71.4%) as well as the fact that in the case of individuals who died (both dogs and cats) the survival rate in the group receiving medicated feed and dietary supplement was slightly longer than in the animals of the control group.

Renal cat 400 g

RenalVet 60 caps.

Table 3. Dogs used in own research

Description of dogs with chronic renal failure used in own research				
Nr of animal	**age**	**sex**	**breed**	**procedure**
1	9 years	male	King Charles Cavalier	Diet + supplement
2	12 years	male	Cocker spaniel	Diet + supplement
3	9 years	female	West highland terrier	Diet + supplement
4	7 years	female	Bull terrier	Diet + supplement
5	2 years	female	German Shepherd	Diet + supplement
6	1,5 years	female	German Shepherd	Diet + supplement
7	17 years	female	Fox terrier	Diet + supplement
8	13 years	male	Beagle	Diet + supplement
9	16 years	male	mixed breed	Diet + supplement
10	17 years	female	mixed breed	Diet + supplement
11	11 years	female	mixed breed	Diet + supplement
12	6 years	male	Pekingese	Diet + supplement
13	15 years	female	mixed breed	Diet + supplement
14	2,5 years	female	labrador	Diet + supplement
15	8 years	female	mixed breed	Diet + supplement
16	7 years	male	mixed breed	Diet + supplement
17	5 years	male	mixed breed	Diet + supplement
18	10 years	male	mixed breed	Nutritioned with standard feed
19	12 years	male	mixed breed	Nutritioned with standard feed
20	6 years	female	labrador	Nutritioned with standard feed
21	10 years	male	German Shepherd	Nutritioned with standard feed
22	7 years	female	mixed breed	Nutritioned with standard feed
23	8 years	female	mixed breed	Nutritioned with standard feed
24	11 years	male	Dachshund	Nutritioned with standard feed

Deaths of patients noted during own observations resulted mainly from the fact that animals were reported to veterinary surgeries in the III or IV phase of chronic renal failure, i.e. in the advanced stage of the disease.

Not in all dogs and cats diagnosed with CKD, it leads to death (especially if it is diagnosed in phase I or II). Especially in cats, the disease can be very slow. An example of this is confirmed by the results of one of the studies, which included 211 cats with CKD, in whom the creatinine values were sCr> 2.3mg/dL. The average survival period was 771 days (1). The median survival time for third stage and fourth stage cats was 679 days and 35 days (1), respectively.

In our own research, the control group was formed of individuals who, despite attempts to provide them with medicated feed, were unable to receive it. Dogs and cats are often reported to veterinary surgeries due to exacerbation of the disease process. Generally, as they do not want to take the standard feed, they show even greater aversion towards the medicated feed. Therefore, the attempt to change the current feed to the medicated one, before it can stabilize the patient and control the clinical symptoms of the disease, may result in the development of aversion in relation to the medicated feed.

Decrease of appetite and weight loss are the main clinical manifestations of the advanced stage of chronic renal failure in animals (3.8). When they show a reluctance to take the food, the owners often replace the medicated feed with more delicious food (as was the case in own observations), however this can contribute to exacerbating the clinical symptoms of the disease (as a result of increased azotaemia, hyperphosphatemia and acid-base disorder) and, consequently, the deepening of the disease process. If animals do not want to consume the food, such a situation can be perceived by their owners as a significant deterioration of the comfort of life, which may further result in a tendency to consider euthanizing animals. Medicated feed should be introduced to the animals gradually so that they have time to get used to the new product (3.8).

To sum up, the Renal Dog® and Renal Cat® (Vetexpert) medicated feeds and the RenalVet® dietary supplement (Vetexpert) prevent chronic kidney disease, contribute to an improved quality of life and prolonged survival of animals with this illness. They show the highest effectiveness in individuals with the 1st and 2nd stage of the disease, in which the most effective is the prevention of concentration of serum creatinine, urea, phosphorus and SDMA, as well as deepening of proteinuria and reduction of urine specific gravity.

In making the prognosis, clinicians should realistically discuss the essence of chronic renal failure as irreversible disease in conversations with owners of ill animals, and emphasize that there are significant individual differences between animals and between their living environment in relation to survival (6); nevertheless, the use of renal food, as well as and a dietary supplement based on calcium carbonate, chitosan and vitamin D, should always be included in the protocol of treatment of patients with this disease (3.8).

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Table 4. Changes in serum creatinine (mg/dL) concentration in the group of cats in subsequent periods of material collection. The specimens that died during the observation were marked in red.

Nr of animal	I collection	II collection	III collection	IV collection
1	1.21	1.54	1.54	1.58
2	1.9	2.04	2.02	2.12
3	3.13	2.88	3.10	3.33
4	9.53	8.35	demise	-
5	4.79	4.24	7.32	demise
6	2.67	2.12	2.15	2.25
7	2.81	4.62	15.94	demise
8	2.28	2.08	2.42	2.56
9	4.16	7.42	13.94	demise
10	4.11	3.6	2.8	3.32
11	1.85	1.36	1.28	1.44
12	2.77	1.66	3.04	4.18
13	2.02	1.8	2.44	2.38
14	2.68	2.95	4.12	6.23
15	3.03	9.14	demise	-
16	5.24	8.13	demise	-
17	1.84	2.0	3.11	3.23
18	9.86	demise	-	-
19	1.46	1.88	2.55	6.93
20	7.12	demise	-	-

Table 5. Changes in urea concentration (mg/dL) in serum in the group of cats in subsequent periods of material collection. The specimens that died during the observation were marked in red.

Nr of animal	I collection	II collection	III collection	IV collection
1	84.2	79.7	82.0	85.3
2	83.1	75.0	62.2	85.0
3	86.1	73.4	78.4	78.1
4	292.2	225.7	demise	-
5	114.3	164.2	351.7	demise
6	110.6	83.2	86.7	76.0
7	127.3	196.5	431.8	demise
8	94.7	84.2	80.1	85.5
9	89.4	106.5	434.2	demise
10	73.3	99.0	124.5	141.3
11	73.9	54.2	68.5	58.9
12	82.0	87.3	139.7	153.6
13	72.8	49.3	57.1	68.8
14	71.3	72.4	159.6	178.8
15	266.0	312.5	demise	-
16	128.3	177.6	demise	-
17	69.4	122.8	214.9	238.0
18	269.2	demise	-	-
19	88.0	170.4	266.3	295.7
20	318.4	demise	-	-

Table 6. Changes in phosphorus concentration (mg/dL) in serum in the group of cats in subsequent periods of material collection

Nr of animal	I collection	II collection	III collection	IV collection
1	2.58	3.14	3.88	4.63
2	3.12	3.31	4.85	5.26
3	3.57	4.12	5.23	5.18
4	7.92	11.73	demise	-
5	4.87	5.93	13.82	demise
6	5.71	5.40	5.52	6.12
7	5.0	8.24	24.29	demise
8	4.17	4.11	4.85	4.11
9	17.58	21.55	23.6	demise
10	7.44	6.25	6.18	7.12
11	6.21	4.88	5.13	5.49
12	3.51	4.92	5.33	4.53
13	4.20	3.29	4.85	4.90
14	6.23	8.75	10.24	12.61
15	6.81	27.4	demise	-
16	9.22	18.30	demise	-
17	4.72	6.39	8.34	10.25
18	19.46	demise	-	-
19	6.12	10.25	12.10	13.76
20	20.12	demise	-	-

Table 7. Changes in the specific gravity of urine in a group of cats in subsequent periods of material collection. The specimens that died during the observation were marked in red.

Nr of animal	I collection	II collection	III collection	IV collection
1	1.025	1.018	1.030	1.028
2	1.057	1.040	1.042	1.035
3	1.030	1.024	1.024	1.018
4	1.012	1.010	demise	-
5	1.012	1.010	1.012	demise
6	1.016	1.012	1.012	1.005
7	1.008	1.010	1.004	demise
8	1.020	1.026	1.024	1,017
9	1.009	1.008	1.011	demise
10	1.010	1.010	1.010	1.008
11	1.010	1.008	1.008	1.009
12	1.015	1.022	1.013	1.013
13	1.015	1.02	1.01	1.01
14	1.021	1.010	1.004	1.004
15	1.009	1.004	demise	-
16	1.012	1.006	demise	-
17	1.031	1.009	1.007	1.005
18	1.002	demise	-	-
19	1.016	1.011	1.006	1.003
20	1.004	demise	-	-

Table 8. Changes in protein concentration (+, ++, +++) in the urine in the group of cats in subsequent periods of material collection. The specimens that died during the observation were marked in red.

Nr of animal	I collection	II collection	III collection	IV collection
1	+	+	+	+
2	+	+	+	+
3	-	-	-	–
4	+	++	demise	–
5	++	++	+++	demise
6	-	-	-	+
7	++	++	++	demise
8	-	-	-	–
9	++	++	+++	demise
10	-	-	-	+
11	+	+	+	+
12	-	+	+	+
13	-	+	+	+
14	+	++	++	+++
15	+	+++	demise	–
16	+	+++	demise	–
17	+	++	++	+++
18	++	demise	-	–
19	+	++	++	+++
20	++	demise	-	–

Table 9. Change in SDMA concentration (mg/dL) in the cat group in subsequent material collection periods. The specimens that died during the observation were marked in red.

Nr of animal	I collection	II collection	III collection	IV collection
1	11	12	12	14
2	12	12	15	15
3	14	15	15	16
4	15	21	demise	-
5	17	18	23	demise
6	12	12	13	12
7	15	17	17	demise
8	13	14	14	15
9	18	18	22	demise
10	20	19	21	21
11	18	16	16	17
12	24	28	36	32
13	19	20	21	21
14	17	21	26	28
15	19	29	demise	-
16	17	33	demise	-
17	16	22	25	25
18	25	demise	-	-
19	15	20	27	25
20	31	demise	-	-

Table 10. Changes in creatinine concentration (mg/dL) of serum in the group of dogs in subsequent periods of material collection. The animals that died during the observation were marked in red.

Nr of animal	I collection	II collection	III collection	IV collection
1	1.81	4.72	demise	-
2	2.41	1.56	1.72	1.70
3	1.91	1.59	1.73	1.68
4	1.85	1.80	1.83	1.88
5	1.71	1.66	1.71	1.76
6	1.83	1.74	1.90	1.90
7	4.04	4.06	11.1	demise
8	7.94	6.48	11.3	demise
9	4.79	8.09	13.98	demise
10	1.44	1.54	1.63	1.77
11	1.38	1.66	1.83	1.82
12	1.29	1.44	1.58	1.50
13	1.88	2.02	2.14	3.46
14	1.81	1.76	2.44	2.85
15	2.05	2.55	2.56	2.42
16	1.1	0.94	1.38	1.40
17	1.54	1.62	1.66	1.90
18	4.66	9.17	demise	-
19	4.88	15.32	demise	-
20	1.99	6.24	16.72	demise
21	2.10	2.33	2.54	5.32
22	2.15	3.12	18.9	demise
23	1.92	12.58	demise	-
24	1.33	2.14	5.32	5.66

Table 11. Changes in urea concentration (mg/dL) in serum in a group of dogs in subsequent periods of material collection. The animals that died during the observation were marked in red.

Nr of animal	I collection	II collection	III collection	IV collection
1	126.3	199.3	demise	-
2	87.3	66.6	98.3	100.0
3	60.1	96.6	102.3	98.4
4	67.2	87.4	78.7	85.5
5	85.8	81.1	89.4	92.6
6	48.7	75.1	89.2	100.3
7	246.3	268.5	480.7	demise
8	208.4	229.6	381.4	demise
9	187.3	228.5	519.2	demise
10	124.6	88.8	95.1	118.9
11	90.3	97.4	106.3	111.1
12	75.3	84.1	95.2	90.5
13	57.4	173.2	188.1	186.6
14	94.2	122.1	134.2	137.7
15	60.0	73.6	76.8	89.5
16	30.8	32.5	48.6	70.1
17	72.5	59.0	101.7	110.6
18	120.2	412.2	demise	-
19	117.3	315.0	demise	-
20	74.8	283.3	465.7	demise
21	71.4	178.3	322.5	414.8
22	93.6	226.4	514.8	demise
23	68.5	335.1	demise	-
24	111.3	155.6	264.9	

Table 12. Changes in phosphorus concentration (mg/dL) of serum in the group of dogs in subsequent periods of material collection. The animals that died during the observation were marked in red.

Nr of animal	I collection	II collection	III collection	IV collection
1	4.46	12.19	demise	-
2	4.58	5.02	6.37	8.63
3	2.77	6.14	6.10	6.30
4	5.58	4.57	6.45	7.15
5	5.30	7.44	7.03	7.55
6	4.96	5.21	5.55	6.12
7	11.32	13.61	13.82	demise
8	7.17	9.13	14.11	demise
9	6.54	9.40	14.96	demise
10	6.22	8.23	8.78	9.03
11	6.58	8.86	8.44	8.80
12	7.22	6.30	6.44	6.81
13	7.83	6.04	7.98	7.99
14	6.22	6.53	7.77	8.02
15	3.85	3.44	5.12	5.98
16	4.25	5.67	5.13	5.02
17	6.24	9.31	9.18	9.54
18	7.16	15.33	demise	-
19	8.22	17.50	demise	-
20	7.88	14.66	16.32	demise
21	6.37	10.16	13.55	14.70
22	8.15	8.88	15.31	demise
23	6.22	14.73	demise	-
24	6.33	5.97	12.14	14.16

Table 13. Changes in the specific gravity of urine in the group of dogs in subsequent periods of material collection. The animals that died during the observation were marked in red .

Nr of animal	I collection	II collection	III collection	IV collection
1	1.011	1.006	demise	-
2	1.018	1.018	1.016	1.015
3	1.032	1.027	1.022	1.014
4	1.023	1.020	1.021	1.016
5	1.044	1.029	1.020	1.020
6	1.023	1.025	1.020	1.015
7	1.008	1.004	1.004	demise
8	1.015	1.010	1.007	demise
9	1.024	1.009	1.009	demise
10	1.048	1.026	1.028	1.018
11	1.028	1.028	1.025	1.014
12	1.030	1.023	1.016	1.017
13	1.033	1.020	1.018	1.013
14	1.046	1.028	1.010	1.010
15	1.023	1.017	1.013	1.010
16	1.013	1.013	1.015	1.010
17	1.015	1.015	1.015	1.015
18	1.018	1.005	demise	-
19	1.013	1.003	demise	-
20	1.024	1.009	1.005	demise
21	1.026	1.008	1.008	1.003
22	1.020	1.019	1.007	demise
23	1.029	1.03	demise	-
24	1.042	1.014	1.009	1.007

Table 14. Changes in protein concentration (+, ++, +++) in urine in the group of dogs in the subsequent periods of material collection. The animals that died during the observation were marked in red.

Nr of animal	I collection	II collection	III collection	IV collection
1	++	++	demise	-
2	+	+	+	+
3	-	-	+	+
4	+	+	+	+
5	+	+	+	++
6	-	+	+	+
7	+	++	+++	demise
8	++	++	+++	demise
9	+	++	+++	demise
10	-	+	+	+
11	+	+	+	++
12	-	-	+	+
13	-	+	+	++
14	+	+	+	+
15	+	+	+	+
16	-	-	-	-
17	-	-	+	+
18	+	+++	demise	-
19	+	++	demise	-
20	+	+	++	demise
21	+	++	++	+++
22	+	++	++	demise
23	+	+++	demise	
24	+	++	++	+++

Table 15. Change in SDMA concentration (mg/dL) in the group of dogs in subsequent periods of material collection. The animals that died during the observation were marked in red.

Nr of animal	I collection	II collection	III collection	IV collection
1	24	24	demise	-
2	17	17	19	19
3	11	15	16	15
4	14	19	21	18
5	16	18	19	23
6	11	14	16	16
7	19	22	33	demise
8	16	10	27	demise
9	14	17	30	demise
10	15	15	17	18
11	17	17	17	17
12	15	18	19	18
13	11	11	14	16
14	13	17	16	19
15	14	14	16	16
16	11	11	11	11
17	12	13	11	13
18	19	33	demise	-
19	25	27	demise	
20	18	25	33	demise
21	11	21	21	23
22	19	29	29	demise
23	16	22	demise	
24	11	15	18	20

The use of cranberry extract and glucosamine in the treatment of lower urinary tract infections in small animals.

PART I Urinary tract infections in dogs

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In view of the increasing life expectancy of dogs, the problem of chronic infections of the lower urinary tract, especially of the bladder, also increases. We are looking for preparations that can replace chemotherapeutics, intended for the treatment and prevention of bacterial inflammatory conditions in the urinary system in dogs. It seems that the cranberry extract in combination with glucosamine may have a bactericidal and stabilizing effect on the bladder mucosa. The aim of the study was to determine the usefulness of cranberry extract and glucosamine in the treatment of urinary tract infections in dogs.

Urinary tract infection means the colonization by pathogenic bacteria of part or of the whole urinary tract. Under physiological conditions, the urinary system, apart from the final section of the urethra, is sterile, free from bacteria. Urinary tract infection is most often a consequence of the migration of ascending bacteria through the genital tract and the urethra into the bladder. This colonization may further spread to the ureters and kidneys. Bacteria that cause urinary tract infections can come from the lower urogenital tracts or be a part of the intestinal microflora. Rarely, these infections are caused by viruses and fungi. In any case, the urinary tract infection is the result of imbalance between the pathogenicity of the bacteria and the body's defences. Pathogenicity of bacteria is their ability to colonize the mucous membrane, to penetrate tissues and to cause a disease.

Factors of bacterial infectivity include, inter alia, the presence of adhesins, i.e. proteins that bind to urinary epithelial receptors, the production of bacterial endotoxins inducing the main immune response, urease production causing high content of ammonium groups in the urine, facilitating bacterial adherence through damage to the glycosaminoglycan protective layer on the surface of the mucous membrane urinary tract (7, 12). The main germs colonizing the lower urinary tract are Escherichia coli, isolated from 46% of cases of urinary tract infections in cats and 44% in dogs, and Staphylococcus spp. - 9% in cats and 11.6% in dogs (7, 8). A number of defence mechanisms were found to prevent the colonization of bacteria, including proper urination (urine flow, frequent urination, complete emptying of the urinary bladder) and protective barrier of mucous membranes (surface layer of glycosaminoglycans, antibacterial properties of mucous membrane, exfoliation of cells) (7).

Urinary tract infection most often affects older animals (cats over 10 years of age, dogs over 8 years of age). Age-related changes in the spine, stretching, incomplete shrinkage of the bladder to its infestation, less mobility of animals, often obesity, as well as long urine retention in the dog's bladder, rare cleaning of cat litter box or too thin layer of the litter in the litter box tray support the growth of bacteria in the urinary tract, and its infections. In case of acute inflammation of the bladder and / or urethra, body temperature increase is possible, as well as decreased well-being, lack of appetite and painful bladder during palpation. Chronic inflammation often does not cause general symptoms, and urinary symptoms are not as pronounced as described above. The owners report more frequent urinary urgency, pollakiuria, often a foul odor of urine, usually noticeable with episodes of periuria (drops of urine at home). During palpation, the bladder is moderately painful or painless, its wall sometimes noticeably thickened. Interview and clinical examination allow to determine the initial diagnosis of urinary tract infection. At the same time, they enable the exclusion of generalized diseases (evaluation of patency of the urethra, determination of the size of the prostate gland, state of the genital system, injuries, coagulation disorders, diabetes, hyperactivity of the adrenal cortex, etc.). Additional tests - general and microscopic examination of urine sediment, imaging technique (X-ray, ultrasound), and finally urine culture – confirm or exclude urinary tract infections. In urine, there is usually a change in pH in the alkaline direction and the presence of protein. The bacteria, white blood cells, red blood cells, mucus bands dominate in the sediment; there is an increased number of squamous epithelium cells (in inflammation of the urethra) and transitional epithelium (in inflammation of the urinary bladder). Urine culture and testing the antibiotic-susceptibility of isolated bacteria is the best way to choose drugs. Often, the proposal of such a test encounters resistance of the owner of the animal due to the additional costs, also due to the necessity of a quick start of treatment (usually a few days of waiting for the result from the laboratory) makes the owner often abstain from this test, especially when it is the first incident of the disease.

Then, most authors recommend using amoxicillin (may be potentiated with clavulanic acid), ampicillin, cephalexin or potent sulphonamides (1, 6, 7). It is noted that aminoglycoside antibiotics and fluoroquinolones are not routinely used to treat urinary tract infections due to their potentially nephrotoxic effects and the rapidly growing resistance of Escherichia coli to enrofloxacin (5). In chronic or recurrent infections, especially in older animals, it may be necessary to conduct long-term or continuous antibacterial therapy controlled by periodic full urinalysis. Substances strengthening the host's defence mechanisms or preventing bacterial colonization may be used as complementary pharmacological treatment, sometimes as its continuation or alternative.

Clinical studies using American cranberry (Vaccinium macrocarpon Aiton) indicate that extracts from this plant may be used in the prevention and treatment of diseases of the urinary tract, in particular urinary tract infections and urolithiasis. Already in the 19th century, German scientists noticed the positive effects of taking cranberry juice in cases of bladder and urinary tract infections. This was associated with the increase of urine acidity, which inhibits the growth of bacte-

ria that colonize the urinary tract. It was also found that the above effect is connected with the hippuric acid contained in cranberry, showing a strong bacteriostatic effect. In further studies, it was found that urine acidification is not the main mechanism of cranberry action (10, 11). Cranberry extract also contains proanthocyanidin (PAC A2, PAC B2, 3-PAC trimers), which combines with bacterial phimbriae, inactivates adhesins, which prevents adhesion of bacteria to urinary tract epithelial cells. This anti-adhesive effect of cranberry prevents colonization of the bladder by bacteria that cause chronic urinary tract infections, e.g. *Escherichia coli*.

In a study conducted by Moan in 1962, a woman with pyelonephritis was given cranberry juice twice a day at a dose of 190 ml. After 9 months of the experiment, almost no protein and fat were found in the urine. In the first clinical trial with random selection of patients to groups, carried out by Avorna et al. in 1994, after 6 months of dietary supplementation with the cranberry juice, a 50% decrease in the number of bacteria and leukocytes was observed in the urine. In addition, in the group of 72 people taking cranberry, only 8 had to use an antibiotic (10). This proves the clear ability of cranberry juice to counter urinary tract infections.

Glycosaminoglycans (GAG) are part of the mucin layer - the outermost layer of the mucous membrane of the bladder. The main biologically active GAGs are hyaluronic acid, heparin sulphate, heparin, chondroitin sulphate and pentosan sulphate. One hypothesis claims that GAG deficiency results in exposure of the urinary tract and contact with irritating urinary components, leading to epithelial damage and leakage. This causes the exposure and stimulation of the C fibers responsible for the sensation of pain, which results in the release of the neurotransmitter – substance P, activation and degranulation of mast cells and the formation of an inflammatory reaction and edema. This phenomenon, so-called neurogenic inflammation, may contribute to the creation of a vicious circle of pain and disorders in urination (6). In cases of interstitial cystitis in humans and cats, the frequency of urinary excretion of glycosaminoglycans is reduced and the permeability of the bladder wall is increased (6, 12, 13). The most popular, the cheapest one, adapted to the administration per os, is glucosamine - a precursor of glycosaminoglycans included in the extracellular matrix in the mucosa of the lower urinary tract. Its administration reduces the permeability of the bladder wall to bacteria and toxins. It stabilizes the bladder mucosa and also has analgesic and anti-inflammatory effects (3, 13, 14).

The aim of the study was to determine the effectiveness of supplements to diets containing glycosaminoglycans and cranberry extract in the course of urinary tract infection in dogs.

Material and methods

The UrinoVet Dog tablet from VetExpert was used for the study, containing in its composition a stabilized extract of American cranberry, parsley extract and glucosamine.

The study involved 22 dogs of different sex, age and race. The experiment was divided into two stages. In the first, urinary tract infection was diagnosed on the basis of clinical trials and additional tests. In the second stage, the clinical efficacy of Urinovet Dog in sick dogs was determined.

All animals presented symptoms from the lower urinary pathways: pollakiuria, urinary urgency, impaired urination, painful urination, vocalization while urinating, hematuria, periodic foul odor of urine, urine leakage, periura (even to urinate at home), urinary incontinence. Symptoms showed varying severity depending on the duration of the disease, age of the animal - more pronounced in acute condition, milder in older animals, exacerbated during recurrent disease (owners were often reconciled with pollakiuria, periuria, droplet urination and its foul odor in older animals, claiming that age has its own rights, and attachment to a dog is stronger than the inconvenience of improper wetting).

The animals were divided into four groups depending on their age and sex:

I – 5 young and middle-aged males (age 2-6 years)
II – 5 young and middle-aged females (age 2.5-7 years)
III – 8 old males (8-12 years)
IV – 4 old females (9-12 years).

Young and middle-aged animals (groups I and II) were not castrated. In the third group 4 males were castrated, in group IV 3 females were sterilized. All dogs were subjected to clinical examination, blood tests: both morphological and biochemical (alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, urea, creatinine, glucose), as well as general urinalysis and urine sediment analysis. Ultrasound examination was also performed.

The following diagnoses were made based on the results of the above tests:

Group I:
3 male dogs – acute cystitis (Ia)
2 male dogs – chronic, recurrent cystitis (Ib)

Group II:
4 female dogs – acute cystitis (IIa)
1 female dog – chronic recurrent cystitis (IIb)

Group III:
5 male dogs - chronic recurrent cystitis (IIIa)
2 male dogs - phosphor ammonium-magnesium urolithiasis / struvite urolithiasis (III b)
1 male dog – oxalic acidosis/ oxolithiasis (IIId)

Group IV:
3 female dogs – chronic cystitis (IVa)
1 female dog – phosphor ammonium magnesium urolithiasis / struvite urolithiasis (IVb).

UrinoVet Dog was the only preparation given to sick animals without additional treatment. It was used for 3 weeks in the amount recommended by the manufacturer - 1 tablet / 5 kg of body weight for acute cystitis and 1 tablet / 5 kg body weight for 6 weeks (42 days) for chronic cystitis and urolithiasis. The preparation was mixed with moist dog food or administered directly to the mouth. All dogs participating in the study were subjected to a weekly clinical control. A full urinalysis with sediment was also performed on day 1 of the study (before administration), day 21 and day 42 of the study, regardless of the time of preparation. In the urinalysis, particular attention was paid to the presence of protein, leukocytes and bacteria. Urine for the test was taken by the owners to a sterile container during the micturition, from the central urine stream. The interview with the owners of animals was very important in assessing the improvement of health. They were asked to pay attention to the frequency of urination, the amount of urine passed, the presence of periuria and the smell of urine. The willingness to take medicine by animals was also important.

The scheme of the experiment is presented in Table 1.

Test results

There was no fever in any of the patients. Dogs with acute cystitis showed painful bladder, involuntary urination while palpating. In dogs with chronic cystitis, thickening of the bladder wall was found during palpation. The owners reported some drops of urine at home, sometimes with a foul odor.

UrinoVet Dog was very willingly accepted by sick dogs. The owners did not report any problems when it comes to direct intake of the preparation (some dogs ate by hand) as well as after mixing it with food. According to the owners, the most visible clinical improvement was noted in 3 animals (1 Ia, 2 females IIa) with acute cystitis. Already after one week, the frequency of soaking decreased (from 8-12 to 3-4 during the day). The symptoms of urinary urgency and painful difficult urination (dysuria) disappeared. In 3 animals (2 male dogs Ia, 1 female dog IIa) with acute cystitis, the improvement was not so pronounced - the frequency of soaking (6-8 times / day) decreased, but there was a slight periuria and dysuria. At the owners' request, after 14 days of using the preparation, an antibiotic (amoxicillin / clavulanic acid) was additionally used. In 1 animal (1 female dog IIa) there was no improvement - pollakiuria, dysuria, stranguria

Photo 1.
Author: Grażyna Wocial-Ziętek

Table 1. Scheme of the experiment.

Group	Number of animals		Diagnosis	Time of administration (days)	Clinical test, urinalysis
I	a	3	acute cystitis	21	1st, 21st, 42th day
	b	2	chronic, recurrent cystitis	42	
II	a	4	acute cystitis	21	
	b	1	chronic, recurrent cystitis	42	
III	a	5	chronic, recurrent cystitis	42 2 dogs up to now	
	b	2	Phosphate ammonium magnesium	42 2 dogs up to now	
	c	1	oxalate urolithiasis	42	
IV	a	3	chronic, recurrent cystitis	42 2 female dogs up to now	
	b	1	struvite urolithiasis	42 to the present	

(painful urination) with vocalization at urination, urinary urgency were noted – after one week antibiotics, anti-inflammatory and diastolic drugs were given and UrinoVet Dog was discontinued. In groups of animals with chronic cystitis (Ib, IIb, IIIa, IVa), clinical improvement consisted in a decrease in the frequency of urinating (from 6-8 to 4-5 per day), resolution of periuria and droplet urination, urine leakage at home.

A noticeable improvement occurred in both male dogs from groups Ib, 2 male dogs from group IIIa and 2 female dogs from group IVa. In the remaining animals (3 male dogs IIIa, 1 female dog IIb, 1 female dog IVa) there was no clinical improvement. In dogs with struvite urolithiasis, treatment by preparation with cranberry and glucosamine was a complementary treatment of urolith dissolution by a diet. In these patients (2 male dogs IIIb, 1 female dog IVb) a relief of urinary symptoms, e.g. no urinary leakage and hematuria, was noted after 3 weeks of supplementation with the preparation. Taking into account that there has been no improvement in a dog with oxolithiasis (IIIc) and inability to dissolve the urolith, it was decided to undergo surgical intervention and antibiotic therapy after the procedure.

In the first, preliminary urinalysis (1st day), all dogs showed signs of inflammation of the bladder. During the course of the experiment, the urine test results changed depending on the effects of treatment. These results clearly correlated with clinical improvement or lack of it. The results of urine tests before and during the experiment are presented in tables II and III.

Due to promising clinical and urine results, some owners decided to extend the administration of the product. It is currently administered at a dose of 2.5 mg / kg b.w. In patients with struvite urolithiasis there was also clinical lack of symptoms of urinary tract inflammation. In the urine test a decrease in the number of leukocytes (8-10 HPF), vesicular epithelia (1-5 HPF) and red blood cells (8-10 HPF) was observed. The number of phosphate crystals dropped to approx. 10 HPF. The owners decided to continue using the preparation until the uroliths were completely dissolved.

Explanation

The product mixed with moist food or delivered directly to the mouth was eagerly consumed by animals. During the course of the study, no side effects were observed. The product slightly increased water uptake by dogs, which gave a beneficial effect supporting its action by increasing diuresis and leaching of harmful substances from the lower urinary tract.

In animals with acute cystitis, the preparation proved to be effective - a visible improvement in 3 animals was observed, which is 42.8%. In 3 patients from this group, the preparation was not so effective, there was an incomplete clinical improvement - slight periuria and dysuria persisted. Because after 14 days an antibiotic was given, it is difficult to say whether these dogs were administered according to the manufacturer's recommendation – after 21 days – there would be a complete clinical improvement. In one dog the preparation turned out to be ineffective after one week. Because administration of UrinoVet was discontinued, it is also difficult to determine its potential effectiveness after prolonged administration. In the group of animals with chronic recurrent cystitis, a marked improvement was noted in 6 out of 11 dogs (54.5%). The measure of improvement, according to the owners, was a reduction in the frequency of urinating and above all the disappearance of the foul odor of urine. One of the positive effects of taking cranberry extract is a significant reduction in urine pH, resulting in the disappearance of unpleasant smell. This is, apart from reducing the symptoms of urinary incontinence, the main noticeable advantage of using cranberry preparations in humans (2, 11). This was confirmed by the urine test on the 21st day of the application when the urine pH decreased significantly.

Lowering urine pH is not the only feature of cranberry extract effect. Habash et al. in a special flow chamber investigated the ability of adherence, i.e. adhesion of bacteria that cause urinary tract infection to the surface of silicone (the basic material of urinary

catheters). In the urine samples obtained after using the cranberry preparation, the adhesion (to plastics) of *Escherichia coli* and *Enterococcus faecalis* granules was decreased in comparison to the control urine samples. It was considered that a cranberry supplement taken as an additive to the diet may limit the adhesion of some microorganisms to the surface of the catheters (9). According to the current state of knowledge, urinary tract infections in humans are caused in 85% of the cases by *Escherichia coli bacilli*. As mentioned earlier, this percentage is 44% in dogs, so it is not a problem to be disregarded in these animals as well. Cranberry extract is nowadays a commonly used preparation in human urology. In the medical literature, one can also find sceptical reports referring to the use of cranberry extracts in urology. Attention is drawn to the results of tests that deny the therapeutic effect of cranberry, but its strongly supportive action in the treatment of urinary tract diseases has not been questioned (10, 11).

Glycosaminoglycans have an important role in protecting the surface of the bladder wall from the harmful effects of urinary components. They prevent adhesion to epithelial cells and infiltration of the bladder wall by microcrystals, proteins, bacteria and even cancer cells. They have antibacterial and anticancer effects and prevent the formation of uroliths. These properties are due to the binding of water molecules on their surface. It is this water layer that creates the environment separating cells from hypertonic urine. This feature is the result of the specific structure of these compounds (14). Attention is drawn to the role of glycosaminoglycans in the pathogenesis and treatment of interstitial cystitis in humans and the similarity of this disease to the idiopathic feline lower urinary tract disease (FLUTD) (3, 8). The possible analgesic and anti-inflammatory effect of glycosaminoglycans in cats is pointed out. In the United States, studies are ongoing to treat FLUTD using GAG (4). Glycosamine is an amino sugar that is part of proteoglycans, which in turn builds cartilage tissue and gives it hardness and elasticity. Orally administered, glycosamine stimulates endogenous synthesis of glycosaminoglycans and hyaluronic acid. Hence, the main use of glycosamine in the prevention and treatment of diseases of the locomotor system in dogs. There are no reports on their use in dog urology.

Positive results of the obtained studies may indicate the beneficial role of both cranberry extract and glycosamine in the treatment of diseases of the urinary tract in dogs. The problem of recurrent bladder infections or permanent, exacerbating subclinical cystitis affects many animals, especially older ones. The lack of side effects of the preparation and the possibility of preventing the recurrence of bladder inflammation/cystitis may be an indication for the use of UrinoVet Dog. In view of the increasing life expectancy of dogs, the problem of urinary tract infections will increase, and preparations with cranberry and glucosamine may be an alternative to antibiotics.

Table 2. Urine test results in dogs with acute cystitis.

Parameter	1st day	21st day	42nd day
Sediment abundant	abundant, cloud-shaped, white	white very poor	very poor
pH	7-9	5-6	5-6
Specific gravity	1035-1050	1030	1030
Protein	3 g/l	-	-
White blood cells	20-50 HPF (per high power field)	5-10 HPF	1-2 HPF
Fresh red blood cells	10-20 HPF (1 female dog lb hematuria)	0-5 HPF	0-2 HPF
Red blood cells leached	numerous	single	-
Bacteria	very few	isolated	single
Transitional epithelium	10-25 HPF	2-4 HPF	2-4 HPF
Crystals of ammonium magnesium phosphate	-	-	-

Table 3. Urine test results in dogs with chronic cystitis and struvite urolithiasis.

Parameter	1st day	21st day	42nd day
Sediment abundant	abundant, compacted, yellowish	Quite poor, white	Quite poor, white
pH	8-9,5	7-8	7-7,5
Specific gravity	1025-1040	1030	1035
Protein	3 g/l	1 g/l	1 g/l
White blood cells	20-40 HPF	10-20 HPF	10-15 HPF
Fresh red blood cells	15-20 HPF	5-10 HPF	5-10 HPF
Red blood cells leached	20-40 HPF	10-15 HPF	10-15 HPF
Bacteria	very numerous	quite numerous	numerous
Transitional epithelium	20-40 HPF	10-12 HPF	8-10 HPF
Crystals of ammonium magnesium phosphate	15-20 HPF	10-15 HPF	5-10 HPF

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The use of cranberry extract and glucosamine in the treatment of lower urinary tract infections in small animals.
PART II. Urinary tract infections in cats

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Infection of the lower urinary tract in cats mostly concerns older animals. It is mainly caused by *E. coli and Staphylococcus spp.* An alternative to commonly used antibiotics may be preparations containing cranberry extract with antimicrobial activity and glucosamine stabilizing the bladder mucosa. The aim of the study was to evaluate the effectiveness of the above-mentioned ingredients in the treatment of lower urinary tract infections in older cats. The first part of the article appeared in MW 8/2010.

An idiopathic feline lower urinary tract disease (FLUTD), also referred to as urinary syndrome, urological syndrome of cats, interstitial cystitis, bladder hematuria or idiopathic cystitis, is a disease that frustrates both the veterinarian and the owner. It is often associated with severe pain of the cat. The cause of this disorder has not been found so far, hence the medical procedure in the field of diagnostics is based on the elimination of other disorders, and the therapeutic procedure - on relieving symptoms and shortening the course of the disease. The term FLUTD (feline low urinary tract disease) refers to all disorders of the lower urinary tract including both urolithiasis and urinary tract infections, reflex dyssynergy (a condition in which the bladder emptying spasm is not accompanied by simultaneous loosening of sphincter muscles) and anatomical changes (congenital malformations, tumors). Possible reasons for this condition include infection. It is believed that bacterial infections are a small percentage of lower urinary tract diseases in cats. Depending on the study, this percentage ranges from 3% to 12-23% (6, 7). As mentioned in part I, the main pathogens colonizing the lower urinary tract are Escherichia coli, isolated from 46% of cases of urinary tract infections in cats and 44% in dogs, and Staphylococcus spp. - 9% in cats and 11.6% in dogs (5 , 6, 7).

Damage to the glycosaminoglycan (GAG) layer is the next considered cause of FLUTD. The protective mechanism of glycosaminoglycans on the bladder mucosa is also presented in part I of the article. The most well-known glycosaminoglycans are hyaluronic acid, heparin sulphate, heparin, chondroitin sulphate and pentosan sulphate. In cats, the use of intravesically administered heparin was tested, but it is both invasive and costly (14). Pentosan sulphate (Cartprophen) available on the Polish market is intended for injection. Glucosamine - a precursor of glycosaminoglycans - administered orally, reduces the permeability of the bladder wall to bacteria and toxins. It stabilizes the bladder mucosa and also has analgesic and anti-inflammatory effects (3, 15, 17).

Some studies have suggested that lower urinary tract disease may be associated with disorders in the nervous system. Elevated catecholamine plasma level concentration was observed in cats with FLUTD. It is believed that their chronic high level may reduce the sensitivity of alpha2-adrenergic receptors, responsible for inhibiting the release of catecholamines and the transmission of painful stimuli to the brain (5, 8, 16). Such receptors are also found in the bladder and are involved in the regulation of blood flow

FLUTD cats are usually 4-7 years old, but there are younger and older individuals which develop the disease. There is a lack of breed predisposition, yet the risk of getting sick is higher in castrated males and smaller in sterilized females. The history is dominated by information about abnormal micturition occurring in about 94% of cats (5, 6, 16). Periuria, hematuria, pollakiuria, painful urination, vocalization while urinating are the most common symptoms. Cats may show a disorder for the first time or the disease may have a chronic, recurrent course. In the absence of severe pain and non-obstructive FLUTD, cats usually maintain their appetite and thirst. During the clinical trial they show normal activity, unless urethral obstruction occurred - then they may show symptoms of postrenal uremia (apathy, vomiting, lack of appetite and thirst).

It is important to determine the size of the bladder. At obstructive FLUTD, an enlarged, tense urinary bladder is palpated, the content of which cannot be squeezed through the urethra (it should be cleared as soon as possible). In cats with non-obstructive FLUTD, the urinary bladder is small, even with gentle palpation, it can lead to micturition due to severe irritation and inflammation of the bladder mucosa. Often, there are no other changes in the clinical trial. The diagnosis of lower urinary tract disease in cats is not easy, because it basically involves the exclusion of other diseases. The exclusion of urolithiasis or urinary tract infections is done by X-ray, ultrasound and urinalysis. Behavioral disorders, the state of the genital system, injuries, coagulation disorders, diabetes, hyperadrenal cortex etc. can be determined by clinical examination, blood tests or interview. Although urinary tract infections in cats are not a big problem, antibiotics are usually given to patients. This is due to waiting for the result of urine culture from the laboratory (usually a few days), the need of treatment or resisting owners against additional costs. Often this is another episode of the disease or a patient with a blocked or partially blocked urethra needs catheterization, performed in an antibiotic cover.

One of the host defence mechanisms against urinary tract infections is to ensure adequate urine flow and frequent urination. The more frequent excretion of urine does not allow prolongation of the exposure time of the urinary tract mucosa to irritating urinary components and enables faster removal of bacteria in the urine. The parsley extract (Petroselinum sativum) has a diuretic effect (increases the volume of urine excreted), which allows to wash away microbes from the urinary tract. Parsley is a natural diuretic (blocks receptors for vasopressin and inhibits the absorption of water in further and

collecting tubules) and induces increased water diuresis. The mechanism of this action is to reduce the activity of the sodium-potassium pump (Na + / K + ATP) in the kidney, which reduces both the reuptake of sodium ions (Na +) and decrease the elimination of potassium ions (K +). This leads to an osmotic influx of water into the lumen of the kidney tubules, increased urine volume and diuresis. Parsley contains essential oil with apiol and myristicin, furanocumarin (bergapten, isoimperatorin), tilts (in fresh herb falkarinol), which in addition to diuretic function also relaxes the smooth muscle of the urinary tract (12).

The aim of the study was to determine the effectiveness of supplements to diets containing glycosaminoglycans and cranberry extract in the treatment of urinary tract infection in cats.

Material and methods

UrinoVet Cat from VetExpert was used for the study, containing stabilized American cranberry extract, parsley extract and glucosamine. The preparation for cats is packaged in sachets. In its composition, it additionally contains lemon balm extract (Melissa officinalis), which soothes and calms the cats with FLUTD, and first of all, deals with idiopathic cystitis, which may have a behavioral basis.

The study included 18 elderly cats (8 females and 10 males over 10 years of age) of different breeds. The research was divided into two stages. In the first stage, the disease was diagnosed in the examined animals based on clinical trials and additional tests. In the second stage, the effectiveness of UrinoVet Cat in the tested cats was determined. All animals exhibited symptoms from the lower urinary pathways - pollakiuria, urinary urgency, difficult and painful urination, vocalization during urination, hematuria, droplet urination, periuria, and urinary incontinence. In some animals, the foul odor of urine was noticeable. All animals were castrated. They were subjected to clinical examination, blood tests: both morphological and biochemical (alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, urea, creatinine, glucose), as well as general urinalysis and urine sediment analysis. Ultrasound examination was also performed.

Based on the results of the above tests were found:

- Gr. I – 8 cats (4 males + 4 females) – cystitiso
- Gr. II – 8 cats (4 males + 4 females) – non-obstructive FLUTD (without clogging of the urethra, 3 cats - the first incident, 5 cats - subsequent relapses of the disease
- Gr. III – 2 cats (2 males) – obstructive FLUTD (first incident) (complete or partial obstruction of the urethra).

UrinoVet Cat was the only preparation given to sick animals. It was administered for 3 weeks (21 days) in the amount recommended by the manufacturer - 1 sachet per day for cystitis (group I), 1 sachet per day for 6 weeks (42 days) with non-obstructive FLUTD (group II) and 2 sachets per day for 5 days in catheters subjected to catheterization with obstructive FLUTD. One cat had catheter left in for 5 days. The preparation was mixed with moist food. Group I cats were subjected to a weekly clinical check-up. Group II cats were examined daily for a week, then as the health improved - once a week for 6 weeks, the cats from group III were also subjected to daily clinical examination for 5 days of administration. A complete urinalysis with sediment was also performed on the 1st day of the study (before administration of the preparation), on the 21st and 42nd day of the study, irrespective of the time of taking the preparation; in cats from group III on day 5 of the preparation administration. Urine for the test was taken by the owners to a sterile container, usually from a cuvette or obtained during the micturition during the clinical examination. In group III it was taken directly from the catheter or by the owners. The interview with the owners of animals was very important in assessing the improvement of health. They were asked to pay attention to the frequency of urinating, the amount of urine, periuria and hematuria. The willingness to take medicine by animals was also important.

The scheme of the experiment is presented in Table 1.

Test results

There was no fever in any of the patients. In cat groups I and II, bladder pain was found - in group I, the bladder was slightly filled with urine, weakly painful, with thickened walls, in group II a small reactive bladder - the animals urinated with a stream or drops during the examination. In 5 cats from this group (4 males + 1 female) haematuria was found. Both in cats from I and II groups, appetite and thirst were preserved. Cats did not show signs of mood worsening. In cats from the III group there were clear symptoms of urethral obstruction - a full bladder with painful walls, strong urinary urgency combined with vocalization. In one cat, a droplet "squeezing" of urine with blood was found. According to the owners, the animals did not eat or drink. In the urine test in cats from group I there were symptoms of subacute cystitis - increase of pH, presence of protein, leukocytes, bacteria, transitional epithelia and mucus. In 3 cats from group II in the urine, single leukocytes were found, fresh and leached red blood cells and vesicular epithelia. In 5 cats with vesicular haematuria in the urine sediment a very large number of fresh red blood cells (covered field of view) were found. In the urine of cat III group acid urine pH, increase in specific gravity, presence of protein in the urine, fresh and leached red blood cells, mucus and polygonal and oval epithelium were found. The urine test results are presented in Tables 2-4.

UrinoVet Cat was readily received by sick cats. In cats from group III, the appetite was restored after about 12 hours after the urethra clearing. In group I, a clear clinical improvement was noted after one week in 3 cats (1 male + 2 females). Frequency of urinating was limited, the animals did not urinate, the owners did not notice polyuria, the foul odor of the urine disappeared. Appetite, thirst did not change, but the animal's mood was better (merrier, more willing to play, looking for a contact with the owner). In a clinical study, the urinary bladder was painless, with thickened walls. This clinical condition persisted for 3 weeks of administration and no relapse occurred. In 4 cats from this group (2 males + 2 females) a slight improvement was found - a slight decrease in the frequency of urinating, improvement in well-being, but still periuria incidents and single episodes of vocalization during micturition were observed. Clinical improvement occurred in 2 cats (2 males) after 21 days of use - no urinary urgency, return to normal urinary frequency. In the remaining two females, no further improvement occurred, despite the 42-day use of the preparation. In these cats

Table 1. Urinary tract infections in cats.

Group	Number of animals	Diagnosis	Time of administration (days)	Clinical test (day)	Urinalysis (day)
I	4 + 4	cystitis	21	1st, 7th, 14th, 21st	1st, 21st.
II	4 + 4	non-obstructive FLUTD	42	1st week – daily 7th, 14th, 21st, 28th, 35th, 42nd.	1st, 21st., 42nd.
III	2	Obstructive FLUTD	5	daily	1st, 5th.

Photo 1.
Author: Grażyna Wocial-Ziętek

additional treatment with antibiotic was introduced (clavulanic acid-amoxicillin), as in 1 cat (male), who lacked any clinical improvement after the first week the owner asked for a change in treatment. The urine test result in cats in this group correlated with clinical improvement. Urine pH decreased, protein content decreased, there was a decrease in the number of leukocytes, epithelia and bacteria.

In group II, clinical improvement was noted in 6 cats (3 males + 3 females). In the clinical trial, frequency of urination, urinary urgency and hematuria were regressed. After one week, the symptoms disappeared completely in 3 cats (2 males + 1 female), in the next 3 animals after approximately 2 weeks (14-17 days). These animals took the preparation 42 days without recurrence of the disease - in 2 of them the owners decided to continue the preventive procedure (1 / 2-1 sachet per day). In 2 cats (1 male + 1 female) there was no clinical improvement after the first week of treatment - at the owner's request, it was decided to change treatment. In cats with clinical improvement, an improvement in the urine test was also found – a radical reduction in the number of red blood cells was observed in patients with haematuria.

In group III, after catheterisation of the urethra, there was a two-day episode of pollakiuria and urinary urgency, without vocalization and hematuria, with a progressive improvement in well-being. Strong bladder tenderness persisted for 3 days during palpation. The owners decided to continue the treatment with a dose of 1 sachet per day; with good effects in the future, the dose will eventually be reduced to 1/2 sachets daily. In the urine test, no symptoms of urinary tract infection were found after 5 days of preparation use. In the cat with a catheter, pollakiuria persisted (partly due to the presence of a catheter). Reduction of hematuria, return of appetite and thirst were noticed. The urinary bladder was painless on the 5th day. In the urinalysis, no symptoms of infection were found, few rare red blood cells were present. The urine test results are presented in Tables 2-4.

Discussion

The preparation mixed with moist food was eagerly consumed by animals. During the course of the study, no side effects were observed. The preparation slightly increased the water intake of the cats, which gave a beneficial effect supporting its action by increasing diuresis and rinsing away toxic, harmful substances and red blood cells from the lower urinary tract. In animals with cystitis, the preparation proved to be effective – after the first week there was a visible improvement in 3 animals, which is 37.5%. In 4 patients from this group, the preparation was not so effective, there was an incomplete clinical improvement – slight periuria and dysuria persisted. A clear clinical improvement occurred after 21 days of application, which increases efficacy up to 62.5%. In 2 cats, the preparation turned out to be ineffective after 6 weeks, and 1 week later the treatment was changed. The measure of improvement according to the owners was a reduction in the frequency of soaking and the disappearance of the foul odor of urine. One of the positive effects of taking cranberry extract is a significant reduction in urine pH, resulting in the disappearance of unpleasant smell. This is, apart from reducing the symptoms of urinary incontinence, the main noticeable advantage of using cranberry preparations in humans (10, 11).

In the group of animals with non-obstructive disease of the lower urinary tract a significant improvement was noted in 6 out of 8 cats (75%). The improvement took place after different periods of application. According to many authors, FLUTD is a self-limiting disease - episodes can withdraw spontaneously without any treatment (4, 15, 16). Such a high percentage of the effectiveness of the preparation may indicate that irrespective of the treatment used, the symptoms of the disease would disappear. Perhaps the preparation shortened the time of the disease and accelerated the diminishing of symptoms. The absence of side effects and the fact that the duration of the incidents did not increase is in favor of UrinoVet Cat.

In group III, the preparation with cranberry and glucosamine proved to be effective. Despite the introduction of the catheter and the lack of antibiotic therapy, no symptoms of urinary tract infections were observed. Urinary tract infections in humans are in approximately 85% caused by Escherichia coli. The bacteria ascending through the urethra, colonizes the urinary bladder, where it attaches itself to the mucosa cells and propagates, causing infection of the bladder. In untreated states, E. coli bacteria can enter the kidneys and cause pyelonephritis (1, 2). As mentioned earlier, the percentage of E. coli infections in cats is 46%, so this is not a small problem.

The surface of the transitional cell epithelium is covered with a thin layer of specific organic compounds called glycosaminoglycans. They owe their properties to the binding of water molecules on their surface. They probably protect the surface of the bladder wall from the harmful effects of urinary components, preventing adherence to epithelial cells and infiltration of the wall by microcrystals, proteins, bacteria and even cancer cells. This water film creates an environment that separates cells from hypertonic urine. This feature is the result of the specific structure of these compounds. They are part of the cell membrane, they perform, among others, signaling role, they are also part of the extracellular matrix (17). Attention is drawn to the role of glycosaminoglycans in the pathogenesis and treatment of interstitial cystitis in humans and the similarity of this disease to FLUTD (3). A possible analgesic and anti-inflammatory effect of gycosaminoglycans in cats was demonstrated. However, in the case of cats, both the positive effect on the stabilization of the bladder mucosa and the lack of benefits over the efficacy of the placebo used are mentioned (8, 9, 13).

Summing up the results of the obtained studies, it can be assumed that both cran-

Table 2. Urine test results in cats with cystitis

Parametr	1. dzień	21. dzień
pH	8-9,5	6-7,5
Specific gravity	1050-1070	1040
Protein	3 g/l	1 g/l
White blood cells	20-30 HPF	5-10 HPF
Fresh red blood cells	10-20 HPF	5-10 HPF
Red blood cells leached	10-20 HPF	5-15 HPF
Bacteria	numerous	few
Transitional epithelium	10-15 HPF	5-8 HPF

Table 3. Urine test results in cats with non-obstructive FLUTD (group II)

Parametr	1. dzień	21. dzień	42. dzień
pH	6-7	5-6,5	6
Specific gravity	1040-1060	1045	1050
Protein	1 g/l	-	-
White blood cells	2-10 HPF	5-10 HPF	5-10 HPF
Fresh red blood cells	10-15 HPF multiple erythrocytes in the field of vision	10-20 wpw	5-10 HPF
Red blood cells leached	10-20 HPF	5-15 HPF HPF	5-10 HPF
Bacteria	single	-	-
Transitional epithelium	2-10 HPF	5-8 HPF	2-5 HPF

Table 4. Urine test results in cats with obstructive FLUTD (group III).

Parametr	1. dzień	21. dzień
pH	6	6
Specific gravity	1080	1055
Protein	1 g/l	-
White blood cells	10-20 HPF	5-10 HPF
Fresh red blood cells	10-20 HPF	5-10 HPF
Red blood cells leached	10-20 HPF	5-15 HPF
Bacteria	numerous	single
Transitional epithelium	10-15 HPF	5-8 HPF

berry extract and glucosamine have a beneficial effect in the treatment of urinary tract diseases in cats. The increase in the number of episodes and recurrences of lower catheter disease and the lack of specific guidelines for the treatment of these conditions, as well as the increased possibility of urinary tract infection in old age support the need to keep searching for alterative treatment methods that are acceptable to both cats and their owners.

The lack of side effects of the preparation and the willing acceptance of it by difficult patients, such as cats, may be a recommendation for the use of UrinoVet Cat containing cranberry extract and glucosamine.

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UrinoVet Cat

Contents: 13.6.2 glycerol monostearate, 13.1.6 dried cranberry fruit, 2.20.1 soybean oil, 13.2.8 glucosamine, 2.21.1 soy lecithin.

Additives (g/kg): Extract of parsley (Petroselinum sativum) 52,6 g, 2b Extract of valerian (Valeriana Officinalis) 42,1 g.

Indications: UrinoVet®Cat is used in cats to support the normal functions of the urinary system. Recommended: for patients suffering from or susceptible to feline lower urinary tract diseases including idiopathic cystiti and urolithiasis.

Dosage: 1capsule per day. The capsule twist off or cut and mixed with food or administered directly into the animal's mouth.

Storage conditions: Store in a dry place at room temperature. Protect from direct sunlight. Store in a place out of the reach and sight of children and animals.

Analytical constituents: General protein – 6,24%, crude fat – 31,81%, crude fiber – 4,30%, crude ash (including minerals) – 10,02%, moisture – 2,04%.

UrinoVet Cat Dilution

Contents: 2.20.1 soybean oil, 2.21.1 soy lecithin, 13.2.8 glucosamine, 13.1.6 dried cranberry fruit.

Additives (g/kg): 3c301 DL-methionine 247.52 g, 3a300 L-ascorbic acid 74.26 g, 2b extract of parsley (Petroselinum sativum) 12.38 g, 2b extract of valerian (Valeriana officinalis) 9.90 g, 2b nettle leaf extract (Urtica dioica) 9.90 g, 3a831 vitamin B6 3.61 g.

Indications: UrinoVet®Cat Dilution is recommended to support the urinary tract of cats. Contains urine acidifying substances.

Dosage: 2 capsules daily (i.e. one in the morning and second in the afternoon). The Twist Off capsule could be cut and mixed with food or administered directly into the animal's mouth. Cat should have constant access to fresh water.

Storage conditions: store in a dry place at room temperature. Protect from direct sunlight. Store in a place out of the reach and sight of children and animals.

Analytical constituents: crude protein – 17.5%, crude fat – 54.2%, crude fiber – 0.6%, crude ash (including minerals) – 3.93%, moisture – 1.2%, starch – 5,9%, potassium – 398 mg/100 g, sodium – 0.65 g/100 g.

UrinoVet Dog

Ingredients: 13.2.8 glucosamine, 11.2.10 magnesium stearate, 11.2.1 magnesium oxide, 13.1.6 dried cranberry fruit.

Additives (g/kg): 2b parsley extract (Petroselinum sativum) 90,60 g.

Technological additives: 1E460 microcrystalline cellulose 239 g.

Indications: used in dogs to support normal functions of the urinary system. Recommended: for patients su ering from acute and recurring urinary tract infections (UTI), for all patients undergoing treatment for urolithiasis, irrespective the type of calculus (urates, struvites, oxalate) and surgery to remove the urinary calculi, protectively in patients after the procedure of catheterization.

Dosage: 1 tablet for every 10 kg of body weight.

Storage conditions: Store in a dry place at room temperature of up to 25 degrees Celsius. Protect from humidity.

Analytical constituents: General protein – 5,58%, crude fat – 2,32%, crude fiber – 23,79%, crude ash (including minerals) – 6,86%, moisture – 5,38%.

KalmVet

Components: 2.20.1 soybean oil, 13.6.2 glycerol monostearate, 2.21.1 soy lecithin.

Additives (g/kg): 2b Camomile (Chamomilla recutita) 186 g, 2b Valerian (Valeriana officinalis) 116,3 g, 3c 3.4.1 Tryptophan 46,5 g.

Indications: The product is recommended for alleviating the symptoms of stress and anxiety in animals.

Dosage: Cats and dogs of up to 10 kg of body weight – 1 capsule a day. From 10 to 25 kg of body weight – 2 capsules a day. More than 25 kg of body weight – 3 capsules a day.

Storage conditions: Store in a dry place at room temperature.

Analytical components: Crude protein 13,55%, crude ash 8,99%, crude fat 23,56%, moisture 2,58%.

RenalVet

Contents: 2.20.1 soybean oil, 11.1.1 calcium carbonate, 13.2.8 chitosan, 9.3.1 beeswax, 2.21.1 soy lecithin.

Additives (g/kg): vitamin D3 – 0,002 g.

Indications: A supportive product for dogs and cats with the symptoms of chronic renal failure.

Dosage: Cats and dogs of up to 10kg of body weight – 1 capsule. Dogs of more than 10 kg of body weight – one capsule for every 10 kg of body weight. The tip of the Twist Off capsule should be cut or twisted off and the contents should be mixed with food. The animal should be provided with access to fresh water at all times.

Analytical contents: Crude protein – 6,65%, crude fat – 57,95%, crude fibre – 0,63%, sodium – 10,70 g/kg, potassium – 1,25 g/kg, calcium - 94,9 g/kg, moisture – 0,85%.

Storage conditions: Store in a dry place in a temperature of no more than 20°C. Protect from sunlight and humidity. Store in a place out of the reach and sight of children and animals.

VetExpert Urinary Cat

Complete food for cats. Dissolution and reduction of struvite stone recurrence.

Composition: Dehydrated poultry protein. Rice. Poultry fat. Apple pulp. Fish oil. Corn starch. Hydrolyzed chicken liver. Yeast. Dried whole eggs. Minerals. Cranberries. Inulin (FOS). Mannano-oligo saccharides (MOS). Marigold (lutein source). Methyl sulfonyl methano. Glucosamine. Chondroitin sulphate.

Nutritional additives: Vitamin A 20,000 IU/kg. Vitamin D3 1,750 IU/kg. Vitamin E 700 mg/kg. Vitamin C 400 mg/kg. Iron (Iron (II) sulphate monohydrate) 75 mg/kg. Iodine (Potassium iodide) 3.50 mg/kg. Copper (Copper (II) sulphate pentahydrate) 10 mg/kg. Manganese (Manganous sulphate, monohydrate) 7.50 mg/kg. Zinc (Zinc oxide) 120 mg/kg. Selenium (Sodium selenite) 0.12 mg/kg. L-taurine 2400 mg/kg. DLmethionine (urine acidifier) 2,500 mg/kg.

Technological additives:
Antioxidants: Tocopherol extracts of vegetable oils 100 mg/kg.

Acidity regulators: Sodium bisulphate 7,500 mg/kg. Crude protein 33.0 %, Crude fat 23.0 %, Crude fibres 3.3 %, Crude ash 7.5 %, Calcium 0.90 %, Phosphorus 0.55 %, Sodium 0.60 %, Magnesium 0.09 %, Potassium 0.62 %, Chlorides 0.70 %, Sulphur 00.40 %.

VetExpert Renal Cat

Complete food for adult cats. Support of renal function in the case of Chronic renal insufficiency or temporary renal insufficiency.

Composition: Dehydrated poultry protein. Corn. Poultry oil. Corn gluten meal. Rice. Corn starch. Yeasts. Fish oil. Potato protein. Rice protein. Beet pulp. Poultry liver hydrolyzate. Cellulose. Minerals. Marigold (lutein source). Inulin (FOS). MOS.

Nutritional additives: Vitamin A 20,000 IU/kg. Vitamin D3 1,750 IU/kg. Vitamin E 700 mg/kg. Vitamin C 300 mg/kg. Iron (Iron (II) sulphate monohydrate) 75 mg/kg. Iodine (Potassium iodide) 3.50 mg/kg. Copper (Copper (II) sulphate pentahydrate) 10 mg/kg. Manganese (Manganous sulphate, monohydrate) 7.50 mg/kg. Zinc (zinc oxide) 120 mg/kg. Selenium (Sodium selenite) 0.12 mg/kg. Taurine 2,400 mg/kg.

Technological additives:
Antioxidants: Tocopherol extracts of vegetable oils.

Acidity regulators: Sodium bisulphate 5,000 mg/kg.

Analytical constituents: Crude Protein 26 %, Crude fat 17 %, Potassium 0.65 %, Sodium 0.40 %, Crude fibres 4 %, Crude ash 5.75 %, Calcium 0.60 %, Phosphorus 0.45 %.

VetExpert Renal Dog

Complete food for adult dogs for the support of renal function in the case of chronic renal insufficiency.

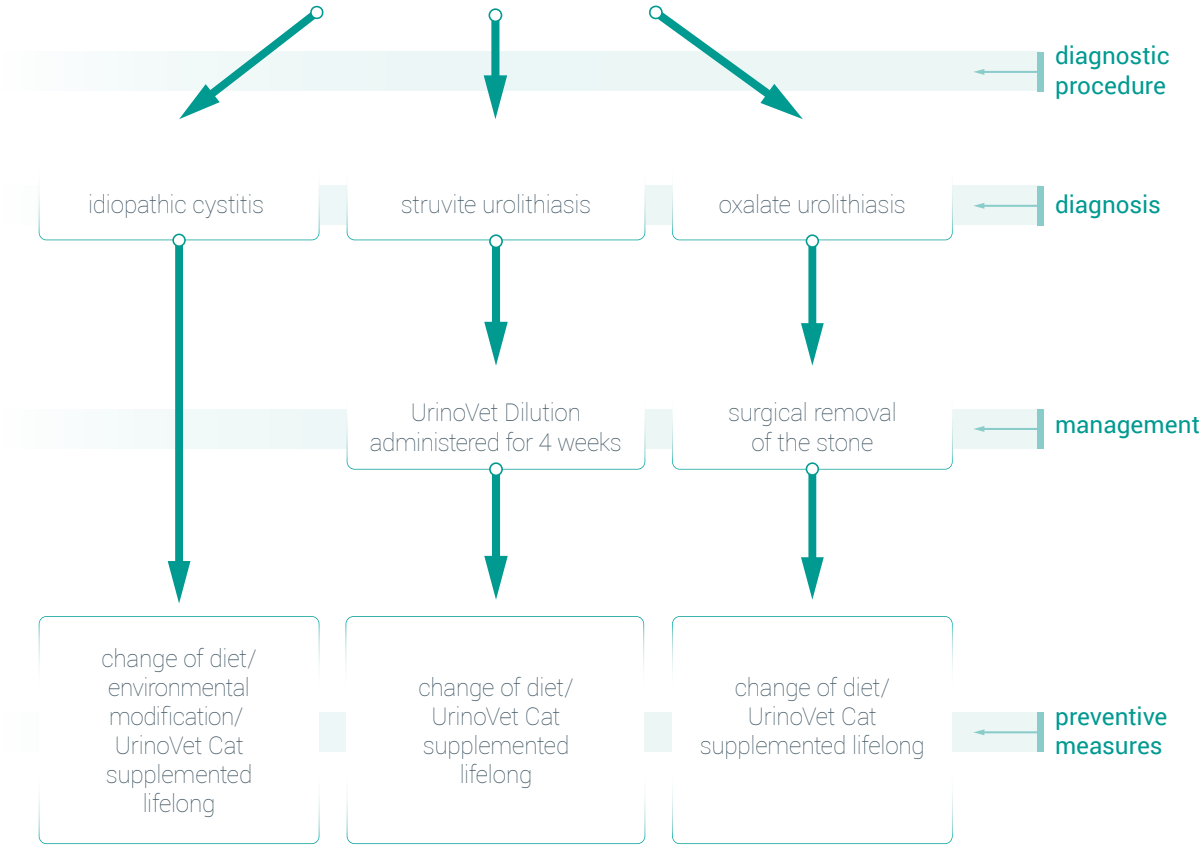
Composition: Rice. Corn. Dehydrated poultry protein. Fresh chicken. Poultry oil. Beet pulp. Corn gluten meal. Yeast. Poultry liver hydrolyzate. Linseed. Cellulose. Fish oil. Inulin (FOS) 7,500 mg/kg. Minerals, Citrus extracts.

Nutritional additives: Vitamin A 18,000 IU/kg. Vitamin D3 1,750 IU/kg. Vitamin E 1,300 mg/kg. Iron (Iron (II) sulphate monohydrate) 60 mg/kg. Iodine (Potassium iodide) 2.80 mg/kg. Copper (Copper (II) sulphate pentahydrate) 8 mg/kg. Manganese (Manganous sulphate, monohydrate) 6 mg/kg. Zinc (zinc oxide) 96 mg/kg. Selenium (Sodium selenite) 0.10 mg/kg. L-carnitine 2,500 mg/kg. Alfa lipoic acid 100 mg/kg.

Technological additives:
Antioxidants: Tocopherol extracts of vegetable oils.

Analytical constituents: Crude Protein 18 %, Crude fat 20 %, Omega-3 fatty acids 1.25 %, Omega-6 fatty acids 3.75 %, Crude fibres 4.5 %, Crude ash 5.5 %, Calcium 0.8 %, Phosphorus 0.5 %, Sodium 0.18 %, EPA+DHA 2,750 mg/kg, Potassium 0.44 %.

Algorithm for the management of suspected feline lower urinary tract disease (FLUTD)



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