



Research reports

A RESEARCH UPDATE
FOR VETERINARY SURGEONS
FROM AFFINITY PETCARE

UROLITHIASIS IN DOGS

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INTRODUCTION

Urolithiasis is one of the main disorders affecting the **urinary tract** and is a routine reason for consultation in the clinic. It is a common condition in dogs where **metabolites eliminated in the urine start to precipitate, leading to the formation of stones**. They are usually of a hereditary, congenital or acquired nature, although they sometimes have a multifactorial or idiopathic origin. Globally, around 3% of dogs are estimated to have urolithiasis. It is essential to determine the type of urolith, as only then we can offer the correct medical, dietary or surgical treatment for each particular case.



MOST COMMON UROLITHS IN DOGS

According to data collected in 2019 by the Minnesota Urolith Center (**Figure 1**), the most common uroliths in dogs are struvite (39%) and calcium oxalate (36%), followed by cystine (6%) and urate stones (purine uroliths) (4%). In a very recent study in Germany¹⁰, struvite (44.7%) and calcium oxalate monohydrate (whewellite, 24.5%) were also among the most common, while the authors also reported a higher prevalence of cystine (15.2%) and ammonium urate (5.3%).

UROLITH COMPOSITION

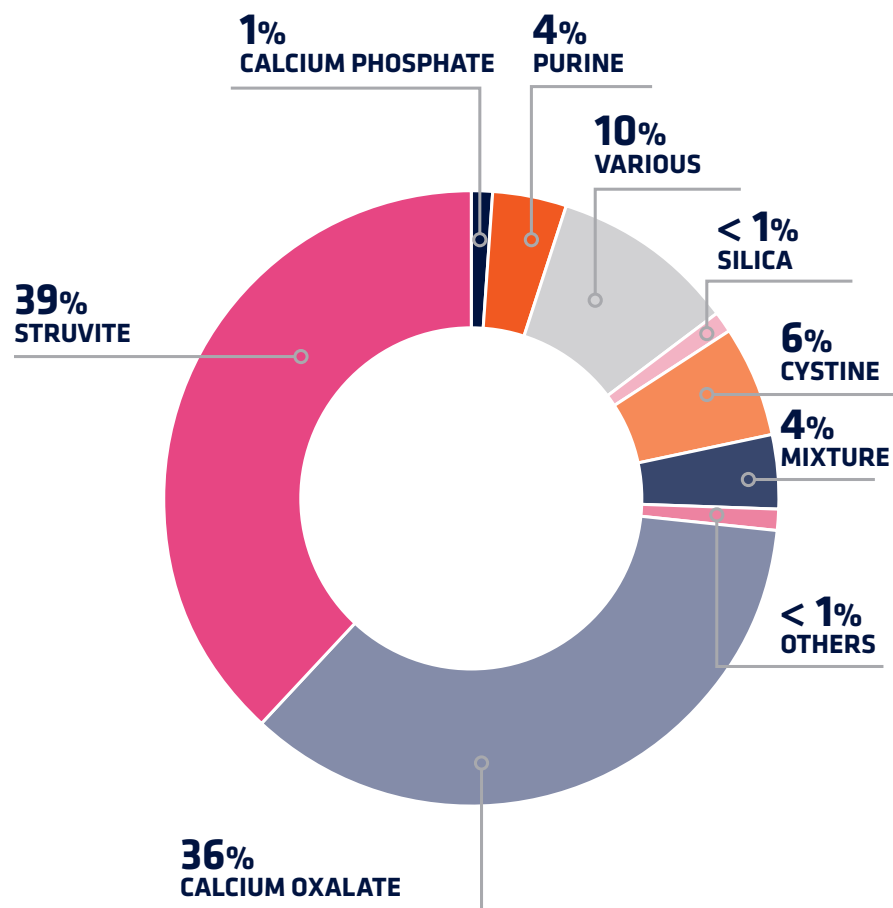
» CALCIUM OXALATE (MONOHYDRATE, DIHYDRATE)

One oxalate molecule bonds with a calcium molecule to form calcium oxalate. The causes of calcium oxalate stone formation are not fully understood. However, their formation is the result of the supersaturation of calcium and oxalate ions in the urine. Other factors that promote the formation of these stones include concentrated urine and an acidic pH. Furthermore, high-molecular-weight proteins in urine also promote the precipitation of these stones. Together with struvite stones, they are the most frequent cause of urolithiasis in dogs.¹ Calcium oxalate stones are considered a chronic disease with a high recurrence rate (50% of cases recur within 2 years).²

» STRUVITE

The main mineral component of these stones is magnesium ammonium phosphate ($\text{NH}_4\text{Mg}^{2+}\text{PO}_4^{3-}$). These stones only form when the urine is saturated with magnesium, ammonium and phosphate. In dogs, most struvite uroliths form after a urinary tract infection involving urease-producing bacteria, such as *Staphylococcus spp.*, *Proteus spp.* or *Enterococcus spp.*³ Urease is an enzyme that converts urea into ammonium, which alkalis urine and therefore promotes the precipitation

FIGURE 1. Mineral composition of uroliths from dogs submitted in 2019 (n = 69,644).



of struvite crystals. Sterile (i.e., in the absence of a UTI) struvite uroliths are common in cats, but rare in dogs.³

» URATE STONES

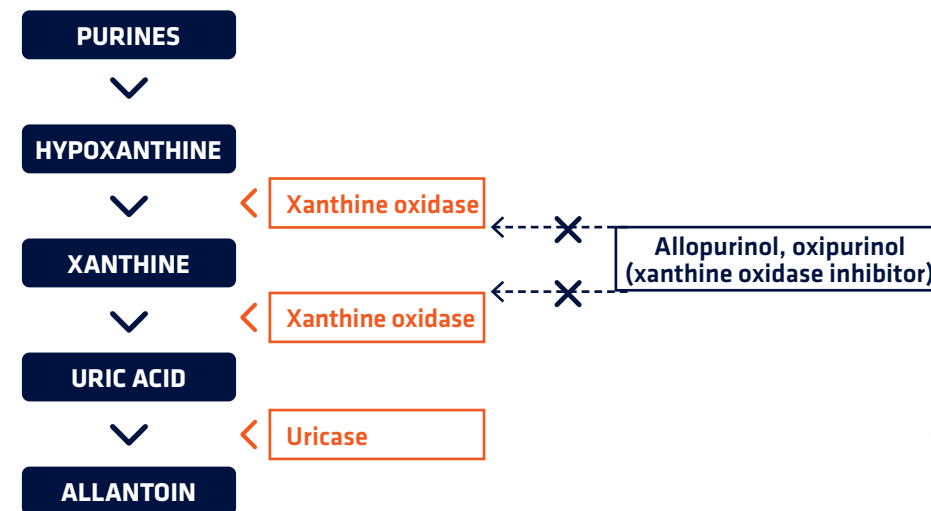
This is the third-most common type of stone in dogs. Uric acid is a degradation product of purine metabolism. In most cats and dogs, uric acid is transported to the liver where it is metabolised by the enzyme uricase to form allantoin, a water-soluble compound that inhibits the formation of urate stones. A defect in the uric acid transporter or impaired liver function (animals with congenital or acquired hepatic vascular abnormalities have a greater predisposition) are leading causes of hyperuricosuria, and consequently

stone formation, in dogs. A defect in the uric acid transporter due to a genetic mutation in the gene SLC2A9 has been reported in Dalmatians, English Bulldogs and the Black Russian Terrier.⁴

» XANTHINE

Xanthine is produced by the degradation of purines in the diet and, under normal conditions, metabolised into uric acid by xanthine oxidase (**Figure 2**). Xanthinuria occurs because of a defect in the enzymes or cofactors that catalyse the final steps of purine degradation. It mainly occurs in dogs affected by Leishmaniasis and being treated with allopurinol or oxipurinol as both medications inhibit xanthine oxidase,⁴ although an idiopathic form has also

FIGURE 2. Purine metabolism.



been reported in some breeds, such as the Cavalier King Charles. These dogs can benefit from a low purine diet, such as **Advance Veterinary Diets Urinary Low Purine**, which helps reduce the risk of xanthine crystal formation. Xanthine stones account for approximately 1.2% of all urate stones and are mostly found in specific breeds including Dalmatian, English Bulldog, Cavalier King Charles Spaniel or Rottweiler.

» CYSTINE

Cystine is an amino acid that is normally excreted in urine, but it is also reabsorbed in the proximal tubules. Cystine starts to appear in urine because of a decrease in its reabsorption. Sometimes this is due to a genetic alteration (genes Slc3a1 and Slc7a9), while in other cases its formation is characterised by an androgen-dependent pattern.⁴

» SILICA

The mechanism of silica stone formation remains unknown. It is believed that there is a relationship between silica stones and the dietary consumption of silicates, silicic acid and magnesium silicate, as the formation of these stones has been associated with ingesting large amounts of corn gluten and soy husks – both rich in silicates.⁴

CLINICAL SIGNS

The clinical signs of dogs with urolithiasis depend on the location of the stones.

Most urinary stones are located in the bladder or urethra and may give rise to clinical signs associated with the lower urinary tract, such as increased urinary frequency, dysuria, urinary incontinence or haematuria. Less frequently, stones can also be located in the kidneys or ureters. In these cases, patients may be asymptomatic, or they could have haematuria and/or abdominal pain.

In addition, urinary stones can physically block the flow of urine (renal pelvis, ureter/s, urethra) causing a urinary obstruction. When there is an obstruction, animals often show signs of azotaemia, hyperkalaemia, metabolic acidosis, dehydration, apathy, vomiting, anorexia, etc.

DIAGNOSTIC ALGORITHM

Diagnostic imaging tests are the technique of choice for confirming the presence of stones in the urinary tract.

• **X-rays** (plain or with contrast) can be used to confirm the presence of



uroliths and determine the number, location, size, radiopacity and shape.

• **Ultrasound** can also be used to detect stones (except those located in the urethra) but it provides limited information on the stones' characteristics.

When they are observed, it is important to perform a complete blood test, which in some cases may suggest the presence of an underlying disease, such as hypercalcaemia or liver problems. A full urinalysis and urine culture with an antibiogram should also be carried out.

By predicting the composition of uroliths before their removal or dissolution, an effective therapeutic plan can be developed that will help prevent their recurrence. The dog's breed and sex can be used as indicators of urolith composition, as can the urinalysis and information obtained from X-rays of the abdomen (radiopacity and stone shape) (**Table 1**). Nevertheless, stones must always be analysed after their removal to determine their mineral composition. And if they recur, the uroliths should be re-analysed, as the mineral composition could change from one episode to another.

• **X-ray appearance of uroliths:** this is one of the best tools for predicting stone composition. Calcium oxalate, calcium phosphate and silica uroliths are radiopaque. Struvite is moderately radiopaque. Other stones, such as those composed of cystine, urate and xanthine, are radiolucent, and contrast X-rays can play a key role in their diagnosis (**Images 1 and 2**).

It is important to bear in mind that stones under 2 mm, regardless of their composition, may be hard to visualise on plain X-rays so other imaging techniques, such as ultrasound or contrast X-rays, are required. On the other hand, radiolucent stones larger than 5 mm may also be visible on plain X-rays.

• **Urinalysis:** urine must be kept at room temperature and analysed within 60 minutes of collection as delaying its analysis and temperature changes could trigger the artificial formation of crystals. Struvite, amorphous phosphate and calcium oxalate crystals are often found in the urine of healthy animals. However, the presence of urate, cystine and xanthine crystals is uncommon and suggests a metabolic disorder. The presence of crystalluria does not necessarily mean there is urolithiasis, and vice versa, the absence of crystals does not rule out the presence of stones. Furthermore, the crystals detected in the urinalysis may not represent the true composition of the stone; as crystals tend to precipitate onto the stone, it lowers the urine concentration of that type of crystal. Urine pH also influences the precipitation of certain stones. Calcium oxalate, urate and cystine all precipitate in acidic media, while struvite and calcium carbonate precipitate in alkaline urine.

• **Breed:** there are certain breed-related predispositions and genetic defects associated with the formation of certain stones. For example, calcium oxalate can appear in any breed, but it is more common in the Schnauzer,

TABLE 1. Characteristics of different types of urolith.

COMPOSITION	RADIOGRAPHIC APPEARANCE	COMMONLY AFFECTED BREEDS	URINE pH
Calcium oxalate monohydrate	Marked radiopacity	Mixed breed, miniature Schnauzer, Shih Tzu, Yorkshire Terrier, Chihuahua, Bichon Maltese	< 6.5
Calcium oxalate dihydrate	Marked radiopacity	Shih Tzu, Yorkshire Terrier, Schnauzer, Bichon, Chihuahua	< 6.5
Struvite	Moderate radiopacity	Shih Tzu, Schnauzer, Dachshund, Pug, Bichon	> 7
Urate	Radiolucent	Dalmatian, English Bulldog, Yorkshire Terrier, Shih Tzu, Schnauzer	< 6.5
Cystine	Radiolucent	English Bulldog, Chihuahua, Dachshund, French Bulldog, Bull Terrier	< 6.5
Silica	Radiopaque	Labrador, Shih Tzu, German Shepherd, Chihuahua, Golden Retriever	-
Xanthine	Radiolucent	Dalmatian, Labrador, Cavalier King Charles Spaniel, Rottweiler	-

IMAGE 1. Retrograde urethrocystography of a dog with multiple urate stones in the distal urethra.

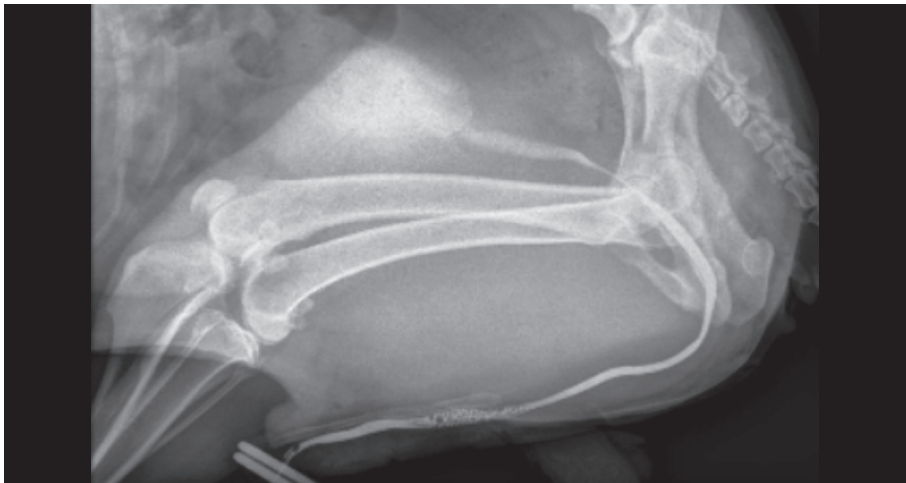
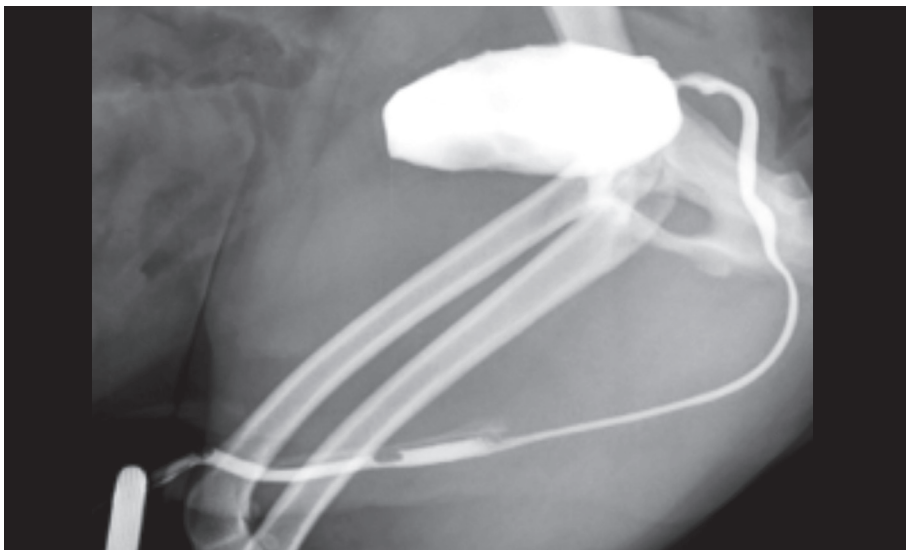


IMAGE 2. Retrograde urethrocystography of a dog with a cystine stone in the penile urethra.



Shih Tzu, Yorkshire Terrier, Chihuahua, Bichon Maltese and Bichon Frise. The English Bulldog often develops urate and cystine stones. In Dalmatians, 96% of stones are urate, mainly affect males and are even more common in entire males.^{1,4}

• **Sex:** calcium oxalate, urate and cystine stones are more common in males, whereas struvite stones are more predominant in females, given the increased risk of urinary tract infections.

• **Age:** calcium oxalate stones are found in more dogs over 7 years old (60%) compared to those under 7 years. In contrast, the prevalence of struvite stones is higher in dogs under 7 (57.5%). In one study, almost two-thirds (62%) of struvite stones occurred in dogs under 4. The proportion of urate uroliths is also higher in animals under 7 years old (62%).

TREATMENT AND PREVENTION

Some types of stone can be dissolved with medical management. Therefore, depending on the suspected type of stone and provided it is not a clinical emergency due to an obstruction, medical management should be attempted before carrying out a more invasive procedure.

» STRUVITE

Medical dissolution is recommended for struvite stones, unless dissolution medications or diets cannot be administered, the uroliths cannot come into close contact with urine or there is an uncontrollable and refractory urine infection (**Table 2**).⁵

» CALCIUM OXALATE

Calcium oxalate stones cannot be dissolved with medical treatment. Consequently, they must be removed physically, with either minimally invasive techniques or conventional surgery.⁵

Oxalate stones have a high rate of recurrence. The recurrence rate is estimated to be 10% during the first 6 months and 35% in the first 12 months,³ so measures should be introduced to reduce the risk of recurrence (**Table 3**).

» URATE

In patients with an Slc2a9 mutation (Dalmatians, English Bulldogs, Black Russian Terriers), medical dissolution should be attempted unless dissolution medications or diets cannot be administered or tolerated, or if the uroliths cannot come into close contact with urine.⁵ **Table 4** summarises the recommendations for the medical dissolution of urate stones and reducing their recurrence.

TABLE 2. Management of struvite stones.

DIETARY TREATMENT (for dissolution)	- Diets with a moderate reduction in protein, phosphorus and magnesium favour the production of acidic urine, thus reducing the precipitation and promoting the dissolution of struvite. - Such diets cause osmotic diuresis because they reduce urea excretion and increase urine volume.
MEDICAL TREATMENT (for dissolution)	Urine infection should be resolved using an antibiotic selected according to the urine culture and antibiogram.
FOLLOW-UP	- The radiographic size of the stones should be assessed every 4 weeks until resolution (usually 8–12 weeks). - The antibiotic treatment must be continued throughout the dissolution process as there are bacteria trapped in the urolith matrix that may be released into the urine as the stone dissolves. The specific diet should be followed for another 4 weeks after the stones have dissolved. The usual diet can be resumed after this period.
PREVENTION	- Struvite stones associated with infection: prevent the recurrence of urine infections and treat them if they appear. - Struvite stones without infection: diets that promote an acidic pH (< 6.5), increase urine output and decrease the excretion of magnesium, ammonium and phosphorus.

TABLE 3. Management of calcium oxalate stones.

DIETARY TREATMENT (for prevention)	- Diets with a high water and low animal protein content as they favour acidic urine and promote diuresis. - Dietary phosphorus should not be restricted as it may induce vitamin D activation and increase the intestinal absorption of calcium. - Avoid a high sodium content as it promotes calciuria.
MEDICAL TREATMENT (for prevention)	- Increase water intake to lower urine specific gravity to below 1.020. - Potassium citrate (75 mg/kg/12–24 h) if urine pH is < 6.5. - Thiazide diuretics, such as hydrochlorothiazide (2 mg/kg/12 h), if calcium oxalate stones recur in the absence of hypercalcaemia, as they increase tubular calcium resorption.
FOLLOW-UP	- Urinalysis every 3–6 months to adjust pH (6.5–8) and urine specific gravity (< 1.020) - Imaging tests every 6–12 months for the early detection of recurrence.

Urate stones associated with a genetic mutation can usually be dissolved after 4 weeks eating a low-purine diet. In one study, complete medical dissolution was achieved in 40% of Dalmatians, partial dissolution in 30% and no dissolution at all in the remaining 30%.⁵ In another study, stones recurred in 50% of dogs consuming low-purine diets, while the recurrence rate was 87% in dogs receiving normal maintenance diets. The best means of preventing urate stone formation in dogs without liver disease is to continue with a low-purine diet.⁵

Urate stones should be removed physically (**Image 3**) and surgical correction of the liver shunt considered in patients with hepatic vascular abnormalities and stones that cannot be dissolved.⁵ However, surgical correction of the vascular anomaly may not be enough to prevent recurrence, so recommendations are to maintain an alkaline pH (pH > 7) and low urine specific gravity (< 1.020) to reduce this risk.

» XANTHINE

In some cases, discontinuing or reducing the dose of allopurinol is enough to resolve xanthinuria and prompt stone dissolution in days or weeks. However, this practice may not suffice for large stones and their physical removal may be required.⁵ **Table 5** summarises the recommendations for reducing the recurrence of xanthine stones.

» CYSTINE

Medical dissolution should be attempted before surgical resection, unless the medication or diet cannot be tolerated or administered, or the uroliths cannot come into close contact with urine, for example, when located in the urethra.⁵ **Table 6** summarises the recommendations for dissolving and preventing the recurrence of cystine stones.

TABLE 4. Management of urate stones.

DIETARY TREATMENT	- Low protein diets resulting in a more neutral or alkaline pH. - Low purine diets as they produce less uric acid. - Diets with a high water content to reduce urine specific gravity (< 1.020).
MEDICAL TREATMENT	- Allopurinol (5–7 mg/kg/24 h) reduces the conversion of hypoxanthine and xanthine into uric acid. Allopurinol should always be supported by dietary treatment. - A certain degree of liver function is needed to convert allopurinol into oxipurinol, so the use of allopurinol is not recommended in dogs with liver disorders. - Potassium citrate (75 mg/kg/12–24 h) if urine pH is < 6.6.
FOLLOW-UP	- Urinalysis every 3–6 months to adjust pH > 7 and urine specific gravity < 1.020. The target is no (or very few) urate crystals in the sediment. - Imaging tests every 6–12 months for the early detection of recurrence. - Allopurinol favours the appearance of xanthine. Therefore, it is important to monitor dogs with urate stones that are given allopurinol in order to rule out the recurrence of urate and/or xanthine.

TABLE 5. Management of xanthine stones or xanthinuria.

DIETARY TREATMENT	- Low protein diet to obtain an alkaline pH. - Low purine diet to reduce xanthine concentration. - Diets with a high water content to decrease urine specific gravity (< 1.020).
MEDICAL TREATMENT	- Eliminate or reduce the use of xanthine dehydrogenase inhibitors (allopurinol). - Potassium citrate (75 mg/kg/12–24 h) if urine pH is < 6.5.
FOLLOW-UP	- Urinalysis every 3–6 months to adjust pH (> 6.5) and urine specific gravity (< 1.020). The target is no (or very few) xanthine crystals in the sediment. - Imaging tests every 3–6 months for the early detection of recurrence. It should be borne in mind that xanthine stones or xanthinuria may occur within a few weeks of starting allopurinol, so closer control may be necessary in the first few months.

IMAGE 3. Urate stones.



» SILICA

Silica stones cannot be dissolved, so they must be removed physically. **Table 7** summarises the recommendations for reducing their recurrence.

PHYSICAL REMOVAL OF STONES

There are several minimally invasive options for removing stones from the bladder or urethra.

In general, small stones that produce clinical signs should be dissolved medically, voiding urohydropropulsion (**Image 4**) or cystoscopy-guided basket extraction.⁵ Uroliths that are too large to pass through the urethra can be eliminated by medical dissolution, lithotripsy or percutaneous cystolithotomy. Whenever these options are unavailable or the stones are large, then traditional surgery (cystotomy) is indicated.

In dogs with uroliths that cannot be dissolved medically but no clinical signs of their presence, it is important to consider the size of the stones. If they are too large to cause urethral obstruction, the situation should be monitored and the owner educated about the potential appearance of associated clinical signs. By contrast, when stones are small enough and likely to enter and obstruct the urethra (stones with a diameter similar to that of the urethra), then they should be removed. The physical removal of stones does not eliminate the underlying cause. Consequently, the additional therapeutic techniques described above are recommended to reduce the risk of recurrence.⁵

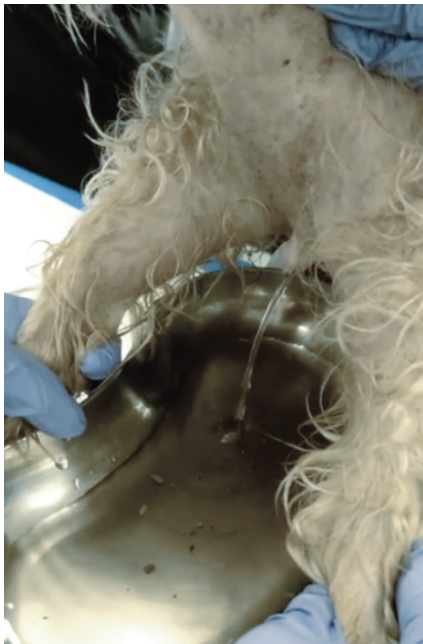
TABLE 6. Management of cystine stones or cystinuria.

DIETARY TREATMENT	- Diet low in animal protein to alkalise urine. - Diet with a high water content to reduce urine specific gravity. - Diet low in methionine, as it is a precursor of the cystine present in animal protein sources.
MEDICAL TREATMENT	Tiopronin (Thiola)* (10–30 mg/kg/24 h) if castration and diet do not reduce cystinuria. *Not available in Spain
SURGICAL TREATMENT	Castration prevents genetic transmission and reduces cystine excretion.
FOLLOW-UP	- Urinalysis every 3–6 months to adjust pH (7–8) and urine specific gravity (< 1.020). The target is no (or very few) cystine crystals in the sediment. - Cystine:creatinine ratio in urine every 3–6 months to determine whether treatment is reducing urine cystine excretion. - Imaging tests every 6–12 months for the early detection of recurrence.

TABLE 7. Management of silica stones.

DIETARY TREATMENT	- Diets with a high water content to decrease urine specific gravity. - Diets with moderate levels of protein to alkalise urine. - Diets with reduced amounts of silica, gluten and whole grains.
FOLLOW-UP	- Urinalysis every 3–6 months to adjust pH (7–8) and urine specific gravity (< 1.020) - Imaging tests every 6–12 months for the early detection of recurrence.

IMAGE 4. Voiding urohydropropulsion.

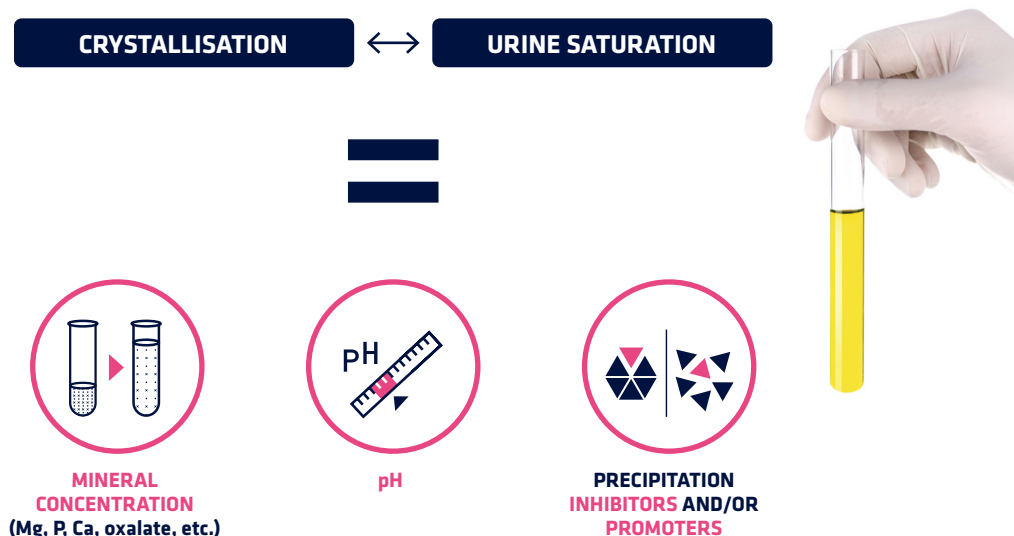


CHARACTERISTICS OF THE ADVANCE VETERINARY DIETS URINARY DIET

CONTROLLED LEVELS OF DIETARY MINERALS

The **calculation of the relative supersaturation of urine (RSS)** is now recognised as one of the best methods for estimating the risk of calcium struvite crystal/stone and/or oxalate stone formation. This method involves using computer software to calculate the crystal's (i.e., struvite or calcium oxalate) activity product. A crystal's activity product is the probability that free compounds in the urine (e.g., magnesium, phosphorus ammonia, calcium, oxalate) combine to form a given crystal (struvite or calcium oxalate), taking into consideration all the possible interactions between all the compounds in urine (e.g., magnesium and citrate).

FIGURE 3. Urine saturation: the most important factor in crystallisation.



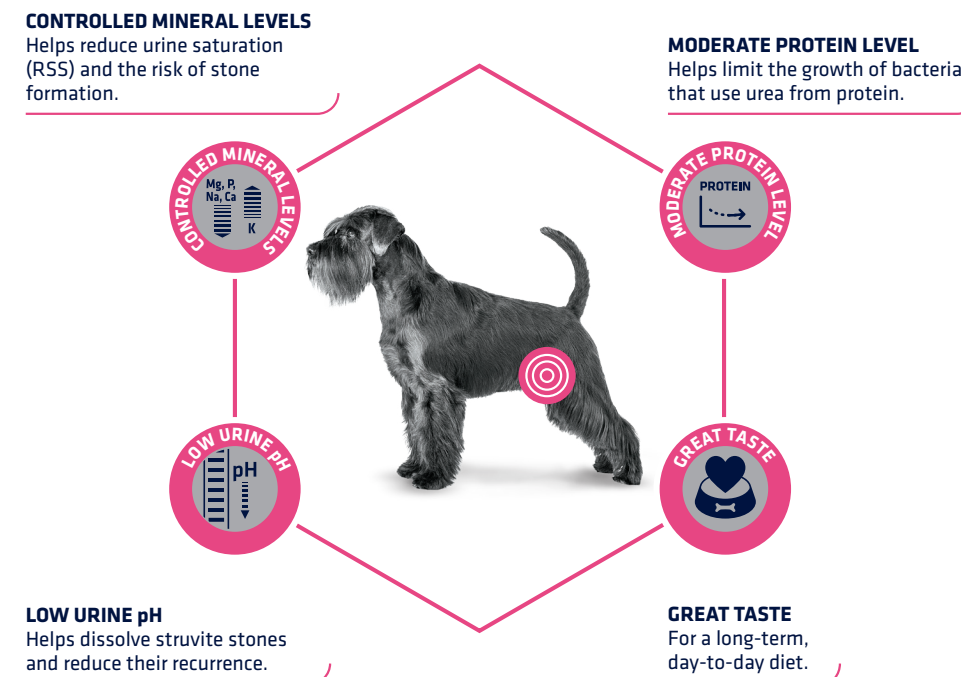
The RSS depends on urine pH (which in turn is influenced by the different minerals present), mineral concentration (influenced by diet, water consumption and the degree of urine dilution) and the presence or absence of precipitation promoters or inhibitors (Figure 3). The RSS indicates whether the urine is **unsaturated** (all crystals present are dissolved), **metastable** (crystals can only form if enough promoters are present), or **supersaturated** (spontaneous crystal formation and growth).

To maintain a low urine RSS, it is important to keep the minerals involved in crystal formation, such as magnesium, calcium and oxalate, at a low concentration in the urine. This can be done by controlling their intake at optimum levels. Alternatively, a low RSS can be maintained by stimulating water consumption and diuresis.

Increased water intake and diuresis importantly help reduce the urine specific gravity (and therefore the

concentration of stone-forming minerals), increasing urine output and, consequently, urinary frequency. This reduces urine transit time and subsequently the time available for stones to form. A wet diet is one option that helps increase water intake.⁵ **Increasing the sodium and potassium content** of dry diets is also known to stimulate water consumption in dogs, thus increasing diuresis and lowering urine density and RSS.^{6,7} However, a high sodium intake can increase calcium elimination and so it may not be recommendable.

The **Advance Veterinary Diets Urinary** diet is formulated with controlled amounts of minerals (calcium, phosphorus, sodium, potassium, magnesium chloride and sulphur) that result in a urine composition that is unsaturated in **struvite** (RSS < 1, which dissolves and prevents the formation of struvite stones), metastable in **calcium oxalate** (RSS < 10, which prevents the formation of calcium oxalate stones) and which maintains a controlled pH.



PROMOTES LOW URINE pH

Urine pH is one of the main factors affecting the RSS of struvite. Therefore, a well-controlled urine pH is key to dissolving and preventing the recurrence of struvite stones, especially when giving dogs dry diets. The pH is less critical in dogs fed wet diets.

The **Advance Veterinary Diets Urinary** diet is especially formulated to encourage a slightly acidic urine pH, which helps dissolve struvite stones and reduce their recurrence.

MODERATE PROTEIN CONTENT

Infections due to urease-positive bacteria are a common cause of infection-induced struvite stones. These bacteria require the urea in urine to grow and proliferate. Reducing dietary protein intake reduces the concentration of urea in urine, hence starving the bacteria of the substrate they need to grow.

Advance Veterinary Diets Urinary is formulated with a moderately low protein content (22%) to help limit the growth of bacteria that use the urea derived from protein.

EXCELLENT PALATABILITY

The food must be very palatable to ensure the dog accepts it, since this is the most important factor in treatment adherence. It is especially relevant for preventing the recurrence of stones, which is best achieved through long-term dietary treatment.



CHARACTERISTICS OF THE ADVANCE VETERINARY DIETS URINARY LOW PURINE DIET

ANTIOXIDANTS FOR THE IMMUNE SYSTEM

Antioxidants have been shown to have a direct effect on the immune system, they can increase or reduce the production of certain cytokines and stimulate certain immune cells. Vitamins E and C are antioxidants capable of neutralising pro-oxidant free radicals. Vitamin E is a fat-soluble vitamin that exercises its antioxidant action at the level of the cell membrane. Vitamin C, on the other hand, is a water-soluble vitamin that with antioxidant action in plasma and extracellular fluid. The antioxidant function of these vitamins partly contributes to correct immune system function by maintaining the structural integrity of important immune cells. Several studies also show that vitamin E increases the production of interleukin 2 (IL-2), a cytokine essential for a correct Th1-type immune response, which increases the

activity of T-helper lymphocytes and stimulates lymphocyte proliferation (it acts as a mitogen by inducing cell division). Furthermore, vitamin E reduces the production of prostaglandin PGE2 (an immune inhibitory factor) and IL-6. Besides its antioxidant function, vitamin C also stimulates the phagocytic activity of leukocytes on the formation of antibodies.

Advance Veterinary Diets Urinary Low Purine contains high levels of vitamin E and C (1300 mg/kg and 350 mg/kg respectively) to contribute to correct immune system function.

EFFECTS OF OMEGA-3 AND 6 FATTY ACIDS, BIOTIN AND ZINC ON THE SKIN

Omega-3 and 6 fatty acids play a role in various skin functions. They form part of the composition of cell membranes and the skin barrier that regulates water permeability and are precursors of pro- or anti-inflammatory mediators, among many other functions. In the case of dermatitis, the patient's diet must maintain an optimal ratio of omega-6 and omega-3 fatty acids to help limit the inflammatory reaction.

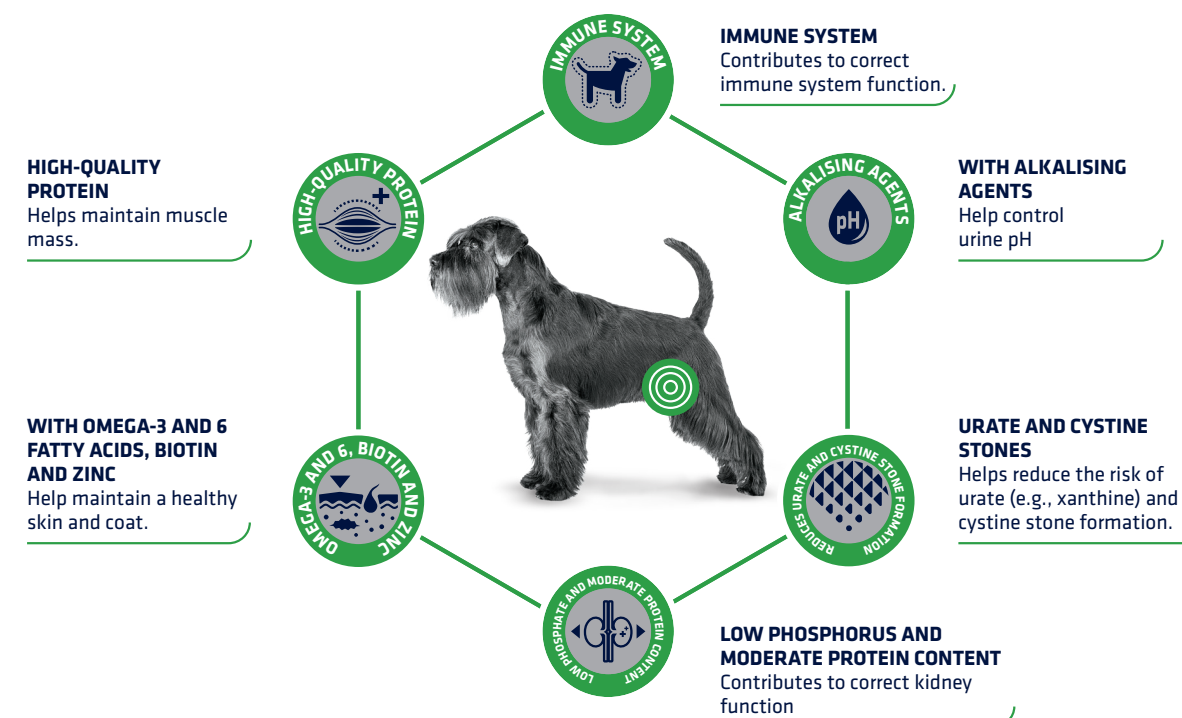
Zinc is an essential trace element required in very small amounts, but it is vital because it helps preserve the integrity of the skin and mucous membranes. It acts as a cofactor in multiple enzymatic pathways and is particularly important for rapidly dividing cells, including skin cells. Zinc is also crucial for fatty acid biosynthesis, participating in both the inflammatory and immune systems, and is involved in vitamin A metabolism.

Biotin takes part in carbohydrate, fat and protein metabolism. In fat metabolism, biotin is necessary for the synthesis of long-chain fatty acids and the metabolism of essential fatty acids that are so important for the skin. Biotin deficiency is known to affect hair formation, paw pads and skin health. **Advance Veterinary Diets Urinary Low Purine has an omega-6:omega-3 ratio of 5:1** and is supplemented with biotin and zinc to help maintain healthy skin and hair.

LOW PHOSPHORUS AND MODERATE PROTEIN CONTENTS

Whenever kidney function is compromised, the **reduced excretion of protein catabolites** significantly helps improve signs of uraemia and many of the other laboratory abnormalities seen in patients with kidney disease. Decreasing the intake of excess or nonessential proteins reduces azotaemia and the production of nitrogenous waste, thus improving the clinical signs. Several studies have shown that a low-to-moderate protein diet, along with a restricted phosphorus intake, is beneficial in dogs with spontaneous or induced chronic kidney disease. This type of diet results in less urea and creatinine in the blood, better maintenance of glomerular filtration rate (GFR) and urine specific gravity (SG), reduced proteinuria, a lower risk of developing hyperparathyroidism, and finally, longer survival times and a reduction in kidney-related deaths.

Advance Veterinary Diets Urinary Low Purine is formulated with a moderate protein (22.5%) and a low phosphorus content (0.55%), which together contribute to correct renal function.



HIGH-QUALITY PROTEIN

When prescribing dogs a low or moderate protein diet, as is the case here, then it is crucial that the **protein is of very good quality**. In other words, it must have a high bioavailability (easily digested and high content of essential amino acids) so that dogs can retain and use as much protein as possible. This means the diet provides enough protein to meet the dog's needs and minimises the production of nitrogenous waste (basically urea) which can have negative effects on the kidneys. Advance Veterinary Diets Urinary Low Purine contains a moderate amount of high-quality protein that ensures a suitable protein intake for maintaining essential biological functions, such as maintaining muscle mass, the skin barrier or a correct immune response, functions which are particularly important in dogs with Leishmaniasis. The diet includes **proteins with a high biological value**, such as egg, milk protein (casein and whey) and **hydrolysed soy protein**.

ALKALISING AGENTS AND pH CONTROL

The solubility of cystine crystals increases exponentially with increasing urine pH. This is why it is so vital that urine has an alkaline pH to prevent stone formation. **Advance Veterinary Diets Urinary Low Purine incorporates alkalisising agents**, such as potassium citrate, which promote a slightly alkaline urine pH and therefore prevent the formation of cystine stones.

PROTEIN SOURCES LOW IN PURINES AND CYSTEINE

Lowering the amount of protein ingested through the diet and selecting the correct protein sources are key to reducing the risk of urate and cystine stone formation in dogs. As such, the formation of urate stones can be prevented by avoiding the use of proteins with a **high content of purines or purine precursors**.



Similarly, since methionine is a cysteine precursor, it is also better to avoid protein-rich diets with a high methionine content.

Advance Veterinary Diets Urinary Low Purine is formulated with a moderate amount of protein from sources selected for their low methionine and purine content to limit the precursors of urate (e.g., xanthine) and cystine stones.

There are also other strategies to prevent the formation of uroliths. One solution involves **increasing urine dilution**. This can be done by **increasing water intake** (e.g., by administering a wet diet) and/or through a protein-restricted diet. Restricting protein intake reduces the concentration of urea in the renal medulla, resulting in greater urine dilution.

DIET SUITABLE FOR DOGS WITH LEISHMANIASIS AND WITHOUT KIDNEY FAILURE

Canine leishmaniasis is an infectious disease endemic throughout the Mediterranean region. The clinical signs are related to the dog's immune response. Affinity Petcare conducted a multicentre study with 21 dogs (mean weight of 24.8 kg and age of 4.5 years) from 6 veterinary clinics in Spain.⁹ The aim of the study was to assess disease progression and changes in lymphocyte distribution with conventional treatment for leishmaniasis combined with a specific diet, such as the **Advance Veterinary Diets Urinary Low Purine** diet. All dogs were diagnosed from their clinical signs and confirmed positive for *Leishmania infantum* by PCR. They were treated with meglumine antimoniate at a dosage of 80 mg/kg/day, allopurinol (Zyloric, GlaxoSmithKline) at 10 mg/kg/12 h and a specific diet with a high antioxidant content, a moderate level of high biological value protein and a low purine content. Clinical and blood

parameters were monitored for 3 months following diagnosis. Immune status was determined by flow cytometry of peripheral blood lymphocyte phenotypes.

After 90 days, the results showed an improvement in the clinical picture: lymphadenopathy returned to normal in 83% of dogs (2/21 vs 12/21), the mean weight gain was 6.3% and body composition score improved by 9%. Analytical parameters also improved: haematocrit (from 36.5% to 43.6%); total platelets (199 to 251·103/μL); C-reactive protein (53.1 to 16.8 ng/mL); γ-globulins (20 to 9.3 g/L); and vitamin E (7.1 to 38.6 μg/mL). The distribution of lymphocyte subsets showed an increase in CD4+ (from 42.8% to 53.3%) and CD4+/CD8+ (1.55 to 2.10), while CD8+ decreased (35.7% to 29.8%).

At the end of the study, the authors concluded that after 90 days of appropriate pharmacological and nutritional support, dogs with Leishmaniasis achieved clinical, haematological and immunological recovery.

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