

KEY POINTS

1

BLUE Natural Veterinary Diet W+U Weight Management+ Urinary Care diet for Dogs and Cats contains controlled levels of magnesium and sodium to minimize the recurrence of struvite urolithiasis.

2

BLUE Natural Veterinary Diet W+U is Clinically Proven:

- To produce a Struvite Relative Supersaturation of <1
- To produce a Calcium Oxalate Relative Supersaturation of <10
- To produce a urine pH of 6.0-6.4

3

BLUE Natural Veterinary Diet W+U was demonstrated to successfully dissolve struvite uroliths in client-owned cats in a multi-center university study.

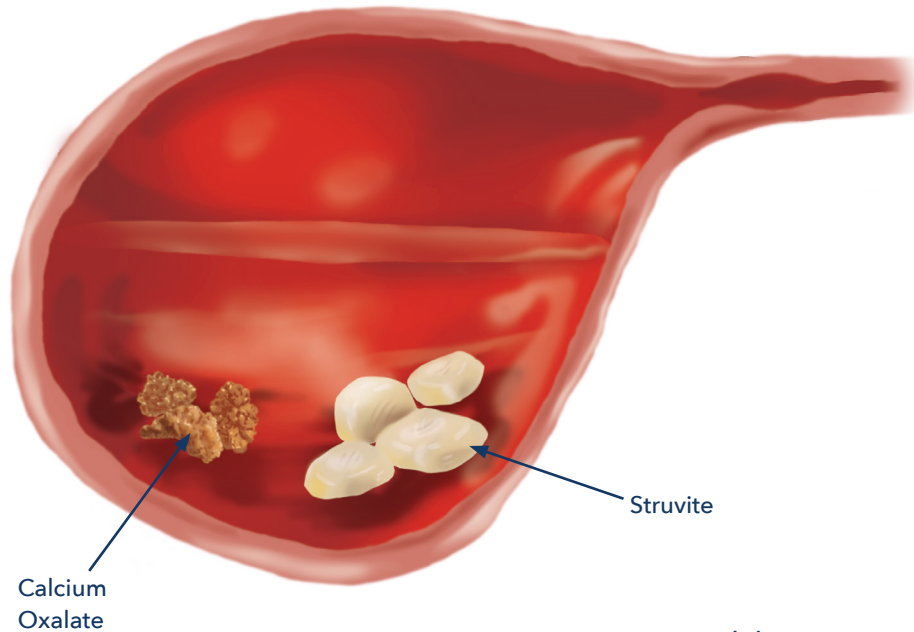
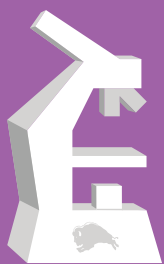


Figure 1. Common Uroliths in Dogs and Cats

Lower Urinary Tract Disease

Urolithiasis is a common disorder of the urinary tract in dogs and cats. Uroliths can form in urine anywhere along the urinary tract from the kidneys to the tip of the urethra causing irritation, infection, pain, and/or obstruction.

The most common canine uroliths are calcium oxalate, magnesium ammonium phosphate (struvite), or mixed.¹ The most common feline uroliths are magnesium ammonium phosphate, calcium oxalate and mixed.^{2,3}

Certain diets, supplements or metabolic conditions can lead to high mineral concentrations in the urine, and potentially stone and/or crystal formation. Urinary pH also influences formation of several crystal types. Although exceptions occur, crystal types tend to form and persist at certain urinary pH ranges. In general, struvite uroliths are associated with more alkaline urinary pH values (>6.4) and calcium oxalate uroliths are associated with lower urinary pH values.^{4,5,6}

In most cases, struvite uroliths form in association with urinary tract infections with urease-producing bacteria (often *Staphylococcus* spp., *Proteus* spp.).^{7,8} Although they are frequent in cats, sterile struvite uroliths rarely form in dogs. The bacteria utilize urea in the urine to form ammonia and carbon dioxide. The ammonia is changed to ammonium, which, in turn, raises the urine pH and becomes available for the formation of magnesium ammonium phosphate crystals (struvite). As the urine pH increases, phosphate becomes more available to contribute to struvite crystal formation and struvite becomes less soluble. As the urine concentrations of phosphate, magnesium, and ammonium rise, supersaturation of the urine occurs, contributing to crystal and urolith formation.^{9,10}

Feline urolithiasis is a common disease seen with equal frequency in both sexes. Until recently, it was thought that most uroliths in cats were small and resembled sand or were

gelatinous plugs that differed from typical uroliths in that they contained a greater amount of organic matrix, giving them a toothpaste-like consistency.⁸ Matrix-crystalline plugs are most commonly found within the urethra near the urethral orifice and are primarily responsible for urethral obstruction. Recently, prevalence of urolithiasis with grossly observable stones composed primarily of calcium oxalate has increased in cats.^{3, 11}

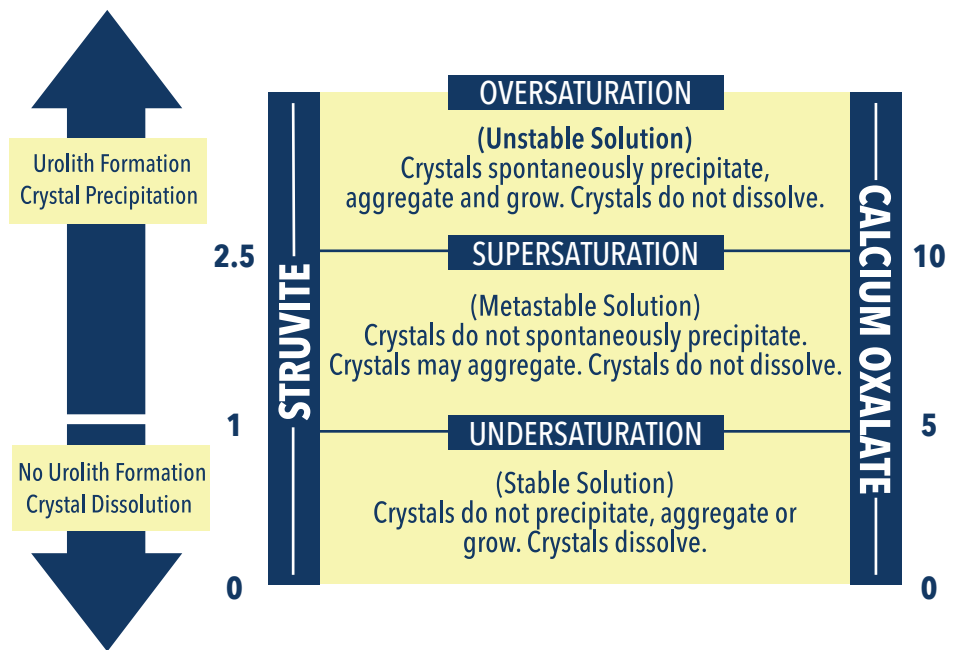
OPTIMAL NUTRITION FOR URINARY SUPPORT

1) RELATIVE SUPERSATURATION (RSS)

Relative Supersaturation (RSS) evaluation has been the gold standard for urine assessment in humans for decades and has been proven to be the only reliable predictor of the risk of calcium oxalate urolithiasis.^{13, 14} This methodology involves the analysis of 12 constituents of a collected urine sample, as well as the determination of urine pH. These data are then analyzed using a computer program that calculates the concentrations of the large number of interactive complexes between all ions present in this urine. Finally, the program calculates the activity product of the urine sample for a given urolith and divides this number by the known constant thermodynamic solubility product for that urolith to determine RSS. Urine below the solubility product for a given salt is termed undersaturated. If urine is maintained within this zone uroliths cannot form. Regardless of the stone type (i.e. struvite, calcium oxalate, etc.) undersaturated urine will have an RSS <1. Any existing struvite crystals or uroliths added to urine in this state will dissolve. Although it is not possible to dissolve pre-existing calcium oxalate, they will not grow or reform in pre-disposed animals in this environment.¹⁵ RSS is a single value that can be used to describe the efficacy of a given diet in managing urolithiasis in dogs and cats.

RSS testing has shown that it is possible for a single diet to manage both types of uroliths (RSS <1 for struvite and RSS <10 for calcium oxalate) (see Figure 2) and that it is possible to undersaturate for calcium oxalate with an acidifying diet.¹³

FIGURE 2. STATES OF URINE SATURATION



STUDY: URINE RELATIVE SUPERSATURATION (RSS) EVALUATION

PURPOSE

To show that feeding BLUE Natural Veterinary Diet W+U Weight Management + Urinary Care food, which contains controlled levels of magnesium and sodium as well as controlled pH levels, can result in clinically significant urine RSS values less than 1 for struvite and less than 10 for calcium oxalate. These RSS values have been shown to limit the formation of struvite and calcium oxalate uroliths and to dissolve struvite uroliths.

STUDY DESIGN

Three groups of adult dogs (n=10 each) and 2 groups of adult cats (n=10 each) were enrolled in the studies. All animals selected were clinically healthy. Animals were maintained in standard, species-appropriate housing and managed consistently during the study, including providing access to activity/exercise. The study protocols were reviewed and approved by the research facility's institutional animal care and use committee.

Animals were fed the species-appropriate dry BLUE Natural Veterinary Diet W+U food for 23 days. An amount of food calculated to maintain body weight was offered once daily and available for 1 hour for dogs and for 20 hours for cats. On day 22, a 24-hour urine sample was collected from each animal, using a metabolism cage with a urine collection system for dogs and a specialized litter box for cats. From that sample, urine pH was measured via pH meter and 2 aliquots were frozen and shipped to The University of Tennessee for RSS analysis.¹⁸ Those aliquots included a 1-ml sample that was diluted with 1.5 ml 1N HCl, and a 10- to 15-ml sample placed in a sterile container. For the RSS analysis, urine sodium, potassium, chloride, calcium, magnesium, phosphorus, citrate, oxalate, ammonia, pH, creatinine, and uric acid were measured.

RESULTS¹⁹

Feeding dry and wet (data not shown) BLUE Natural Veterinary Diet W+U food in both dog and cat studies resulted in clinically proven urine RSS values <1 for struvite and <10 for calcium oxalate.



CHART 1. RSS STUDY RESULTS

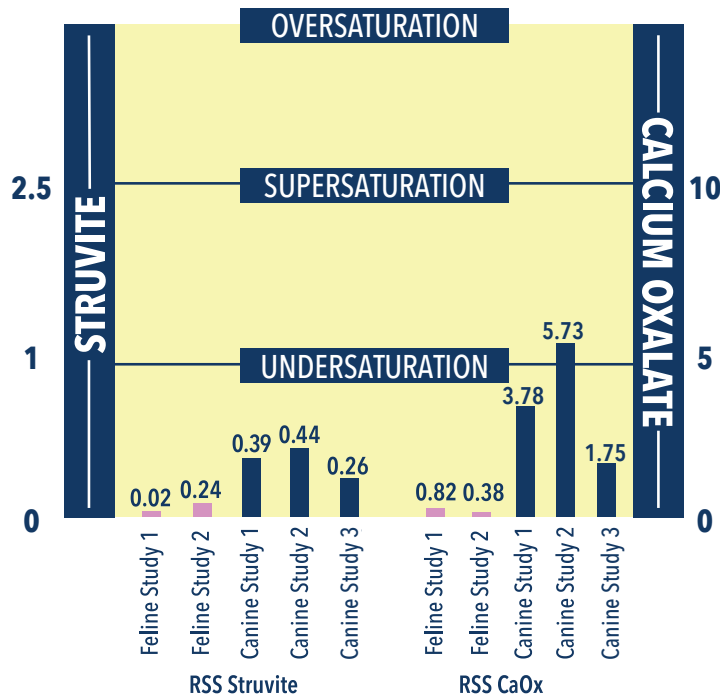
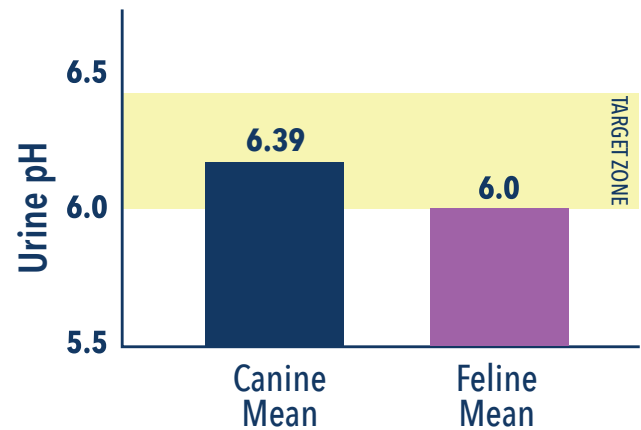


CHART 2. URINE pH MEAN RESULTS



STUDY: FELINE STRUVITE DISSOLUTION CLINICAL STUDY

PURPOSE

To demonstrate the efficacy of BLUE Natural Veterinary Diet W+U Weight Management + Urinary Care in dissolving struvite uroliths in client-owned cats.

STUDY DESIGN

Twelve client-owned adult cats with radiographic and urinalysis results consistent with struvite cystoliths were enrolled in this prospective, open-label, two-center study. Cats were fed BLUE Natural Veterinary Diet W+U Weight Management + Urinary Care dry formula exclusively and were radiographed every other week until urolith dissolution was noted or day 56 was reached. In cats with uroliths still evident at day 56, cystotomy was performed for stone retrieval and analysis.

RESULTS²⁰

Complete dissolution of struvite uroliths was achieved in 8 of the 9 cats that completed the study: stones dissolved as soon as 14 days in 2 cats and within 28 days in 5 cats. One cat, who had partial dissolution at day 56 and whose owner declined cystotomy and continued to feed the diet, had complete dissolution at day 70. Another cat had partial dissolution, with significantly reduction in the size of 2 uroliths at day 56, and had 2 small calcium oxalate urolith cores removed on cystotomy. Overall, in-home feeding of BLUE Natural Veterinary Diet W+U Weight Management + Urinary Care dry formula was successful in dissolving struvite uroliths in cats.

2) Urine pH

Formulating effective medical management for uroliths depends on knowledge of the mineral composition of uroliths. To prevent struvite urolithiasis in dogs and cats, it is important that the food is carefully formulated to consistently produce urine in a tight pH range appropriate for the stone type.

STUDY: URINE pH STUDIES

PURPOSE

To show that feeding BLUE Natural Veterinary Diet W+U Weight Management + Urinary Care food can consistently produce a urine pH of 6.0-6.4, which includes the recommended urine pH ranges to prevent struvite urolithiasis in dogs (6.2-6.4) and cats (6.0-6.4.)

STUDY DESIGN

Four groups of adult dogs (n=10 each) and 2 groups of adult cats (n=8 each) were enrolled in the studies. All animals selected were clinically healthy. Animals were maintained in metabolism cages during the study. Animals were fed the species-appropriate dry BLUE Natural Veterinary Diet W+U food for 7 days. An amount of food calculated to maintain body weight was offered once daily and available for 2 hours. At the end of the feeding period, urine samples were collected from each animal at 0, 4, 8, and 24 hours via cystocentesis for measurement of pH.

RESULTS¹⁹

Overall, feeding BLUE Natural Veterinary Diet W+U food in both dog and cat studies resulted in mean urine pH values between 6.0 and 6.4.

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CLINICAL IMPACT

The results of the studies discussed in this Clinical Report support the effectiveness of BLUE Natural Veterinary Diet W+U Weight Management + Urinary Care in dogs and cats for dissolving struvite uroliths, with clinically proven urine pH of 6.0-6.4 and struvite RSS <1 as well as confirmed radiographic dissolution in feline patients. Additionally, with clinically proven calcium oxalate RSS <10, BLUE Natural Veterinary Diet W+U Weight Management + Urinary Care can reduce the risk of development of calcium oxalate as well as struvite uroliths and support the urinary health of dogs and cats.

For more information about Blue Buffalo Quality Assurance Testing and Clinical Research please visit BLUEVetConnect.com or call 1-888-323-BLUE.



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