Urate Urolithiasis – Canine

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Definition

In ***urate urolithiasis***, uroliths are composed of uric acid or salts of uric acid; ammonium urate occurs most commonly. The condition may occur as a result of liver disease, most commonly portovascular shunt or microvascular dysplasia, or as a metabolic defect without liver disease, most commonly in Dalmatians and English bulldogs.

Key Diagnostic Tools and Measures

In cases associated with portovascular shunt or microvascular dysplasia, clinical and laboratory findings include stunted growth, microcytosis, low-normal or sub-normal BUN, hyperammonemia, abnormal provocative serum bile acid testing, possible signs of hepatoencephalopathy (ptyalism, depression, vomiting, seizures) particularly associated with eating, and urate crystalluria. Urate uroliths are marginally radiodense or radiolucent; identification requires ultrasonography or double-contrast urocystography. Microhepatica may be seen on survey abdominal radiography or abdominal ultrasonography. Contrast portography may reveal shunting of blood if a shunt is present. Portal scintigraphy is abnormal. Identification of extravascular or intravascular hepatic shunt if present is made at surgery.

In cases *not* associated with portovascular shunt or microvascular dysplasia, findings may include hyper-uric acidemia (healthy dogs: 0.1–0.3 mg/dL; with urate urolithiasis, >0.3 mg/dL, usually 0.8–1.5 mg/dL), and urate crystalluria. Urate uroliths are marginally radiodense or radiolucent; identification requires ultrasonography or double-contrast urocystography. Urate urolithiasis may be associated with miliary dermatitis in Dalmatians, and with dilated cardiomyopathy in English bulldogs.

Pathophysiology

Uric acid is a metabolite of purine metabolism from endogenous and exogenous sources. Purines include the nucleic acid bases adenine and guanine. Purines enter into the purine metabolic pathway and are metabolized to hypoxanthine to xanthine and xanthine to uric acid by xanthine oxidase. Uric acid is metabolized to allantoin by hepatic uricase. Allantoin is the typical end-product of purine metabolism in dogs.

Urate uroliths form with urinary oversaturation with uric acid. With liver disease, conversion of uric acid by uricase and ammonia by the urea cycle is decreased. In dogs without liver disease, conversion of uric acid to allantoin is decreased and decreased reabsorption or increased secretion of uric acid by proximal renal tubules occurs.

Urinary and serum uric acid concentrations can be decreased by restricting dietary purine (protein) intake. Dietary protein restriction also decreases ammonia production. Urate uroliths form typically in acidic urine, and decreasing dietary protein intake results in alkaluria.

Signalment

Young dogs, especially those of small breeds (e.g., Yorkshire terriers, miniature schnauzers), are typical signalment for dogs that form urate uroliths secondary to congenital liver disease. Dalmatians and English bulldogs have increased incidence of urate urolith formation without congenital liver disease. Urate uroliths occur more commonly in males, with the highest incidence in 1- to 5-year-old dogs.

Key Nutrient Modifications

Uric acid comes from endogenous and exogenous purines. Exogenous purine sources are highly cellular nutrients, such as animal-based protein sources. Organ meat is particularly high in purine content. Ammonia originates from colonic bacterial metabolism of protein and from ammonia excretion by kidneys. Ammonia from intestinal bacteria is normally metabolized to urea by the hepatic urea cycle. Kidneys excrete ammonia as a buffer for acid by filtration and deamination of glutamine. Dietary protein restriction results in decreased purine intake, decreased ammonia production, alkaluria (uric acid is more soluble in alkaline pH) and diuresis, which results in dilution of calculogenic compounds in urine.

Recommended Ranges of Key Nutrients

Nutrient	% DM	g/100 kcal	% DM	g/100 kcal
	Recommended dietary level		Minimum dietary requirement*	
Protein	14–17	3.0–4.0	18	5.1

Modified intake of these nutrients may help address metabolic alterations induced by disease states. The recommended dietary composition is shown as percent of dietary dry matter (DM) and as g or mg per 100 kcal metabolizable energy. All other essential nutrients should meet normal requirements adjusted for life stage, lifestyle, and energy intake.
*Nutrient requirement for adult animals as determined by the Association of American Feed Control Officials

Therapeutic Feeding Principles

For dogs with urate uroliths, but without liver disease, nutritional management includes feeding a low or ultra-low protein diet that induces alkaluria and diuresis. Crude protein (on an as fed basis) should be 11% to 16% (dry food) and 3% to 4% (canned food). These diets also usually are formulated to contain an alkalinizing agent, often potassium citrate. In theory, a vegetarian diet may be beneficial but this is unproven. A hydrolyzed vegetable protein diet, which does not contain organ meats that are high in protein, can be fed. Nutritional management principles are similar in dogs with urate uroliths and liver disease.

■ **Treats** – Low-protein treats, such as carbohydrates or vegetables, can be fed. Avoid high-protein treats, such as meats or cheeses, or treats that result in aciduria.

■ **Tips for Increasing Palatability** – Adding water to food may increase palatability and result in polyuria that may dilute calculogenic components. Adding light salt (potassium chloride) may stimulate thirst resulting in polyuria that may dilute calculogenic components.

■ **Diet Recommendations** – Low-protein or ultra-low protein diets that are alkalinizing and induce a diuresis, such as renal failure diets and advanced renal failure diets, are recommended. Feed to maintain body weight and body condition.

Client Education Points

For dogs without liver disease:

- Urate uroliths form because of an inborn error of metabolism of uric acid.
- Urate uroliths are highly recurrent without dietary modification and possibly administration of allopurinol, a xanthine oxidase inhibitor that decreases the amount of uric acid in urine.
- Diets formulated for management of urate uroliths are effective, but not 100%.
- Treats even in small amounts can result in recurrence of uroliths and should be given sparingly.

For dogs with liver disease:

- Urate uroliths form due to an underlying liver condition.
- Management of the liver condition, especially if surgical correction of a

blood vessel bypassing the liver, is often curative.
- In other dogs, medical management of the liver disease often helps to prevent recurrence of or formation of urate uroliths.

Common Comorbidities

Hepatoencephalopathy and liver failure are seen in dogs with congenital liver disease and urate urolithiasis. Dilated cardiomyopathy has been associated with urate urolithiasis in English bulldogs and Dalmatians. Dalmatians with urate uroliths often have miliary dermatitis.

Interacting Medical Management Strategies

The xanthine oxidase inhibitor allopurinol competitively inhibits conversion of hypoxanthine to xanthine and xanthine to uric acid, thereby decreasing urinary uric acid concentration. The dosage for dissolution of urate uroliths is 15 mg/kg orally (PO) every 12 hours; for prevention, if used, 7–10 mg/kg PO every 12 to 24 hours can be given. The most common complication is xanthine crystalluria and urolith formation; occasionally dermatitis may occur. Xanthine oxidase is not effective in dogs with liver disease.

The urinary alkalinizing agent: potassium citrate increases solubility of uric acid in urine and decreases urinary ammonia excretion.

In dogs with urate uroliths secondary to congenital liver disease with hyperammonemia and hyper-uric academia, antibiotics (e.g., neomycin, amoxicillin) to decrease intestinal bacterial counts and/or lactulose may be necessary to decrease absorption of ammonia from the intestinal tract. Other treatments to consider include S-adenosylmethionine (SAMe), vitamin E, and milk thistle or silymarin.

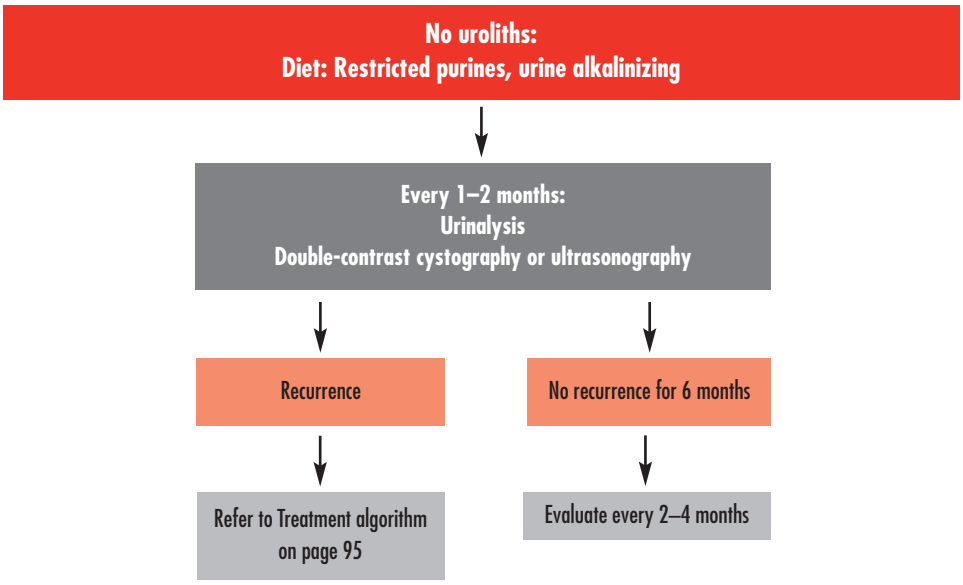
Monitoring

Dogs with urate uroliths but without liver disease should be monitored monthly during dissolution with abdominal ultrasonography or double-contrast cystography and urinalysis (pH should be alkaline, specific gravity should be dilute, crystalluria should be absent). For prevention, for first 6 months following dissolution or surgical removal of uroliths, perform urinalysis every 1 to 2 months (pH should be alkaline, specific gravity should be dilute, crystalluria should be absent). Consider monitoring BUN because low protein intake should result in decreased BUN concentration. Abdominal ultrasonography or double-contrast cystography is recommended at 6 months and 12 months. If no recurrence, consider monitoring urinalysis every 4 to 6 months thereafter unless there is recurrence of clinical signs.

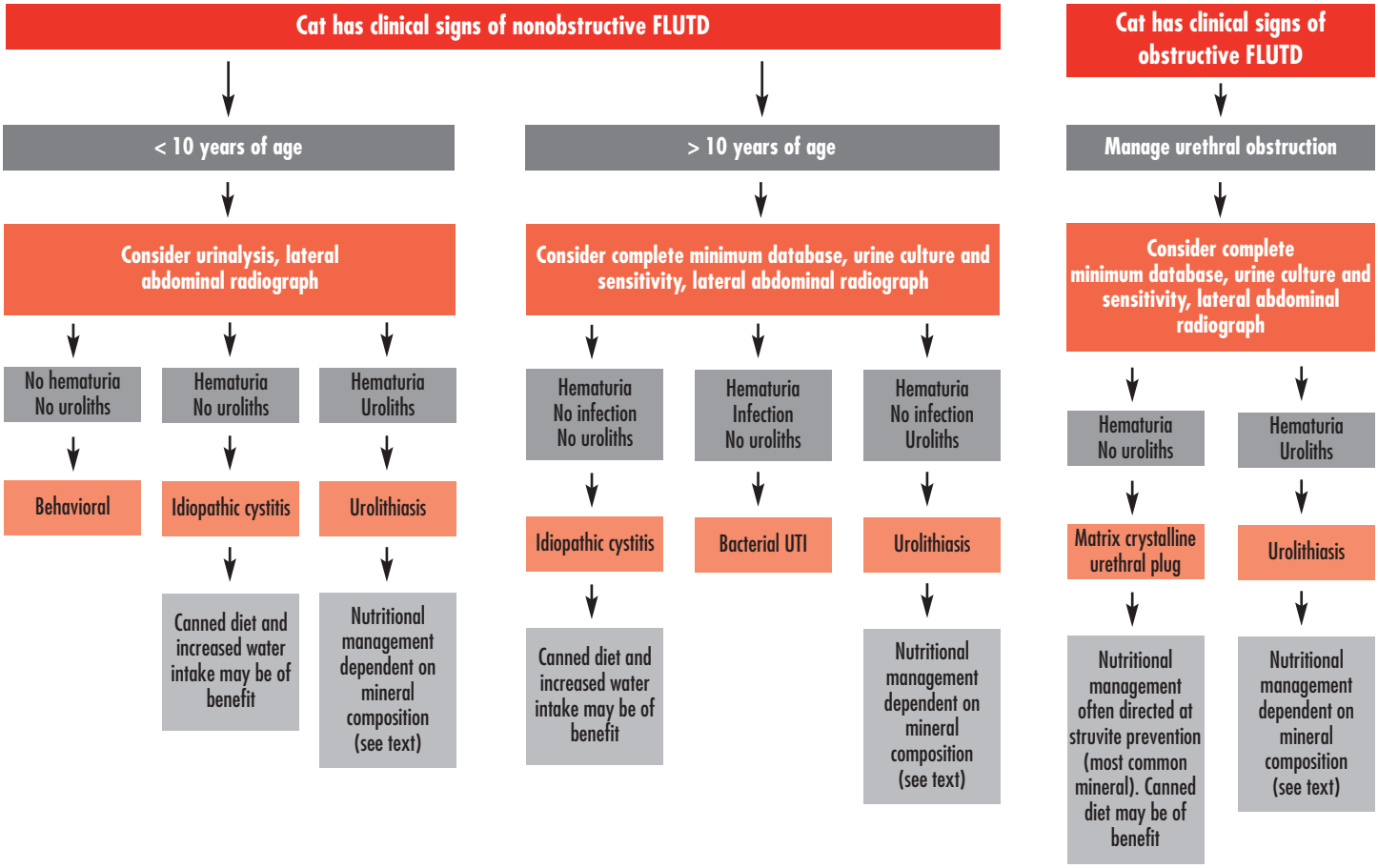
In dogs with urate uroliths and liver disease, if surgical correction of portovascular shunt is possible, no further monitoring may be required as correction of the shunt should eliminate urate urolith recurrence. If surgical correction is not possible, monitoring will depend on severity of clinical signs and response to treatment. Monitor urinalysis and blood work every 3 to 6 months.

See **Algorithm – Nutritional Management for Treatment of Canine Urate Urolithiasis** on page 95.

Algorithm – Prevention of Canine Urate Urocystolithiasis



Algorithm – Nutritional Management of Feline Lower Urinary Tract Disease



Algorithm – Nutritional Management for Treatment of Canine Urate Urolithiasis