

MINNESOTA UROLITH CENTER * University of Minnesota

College of Veterinary Medicine * 1352 Boyd Avenue * St Paul, MN 55108

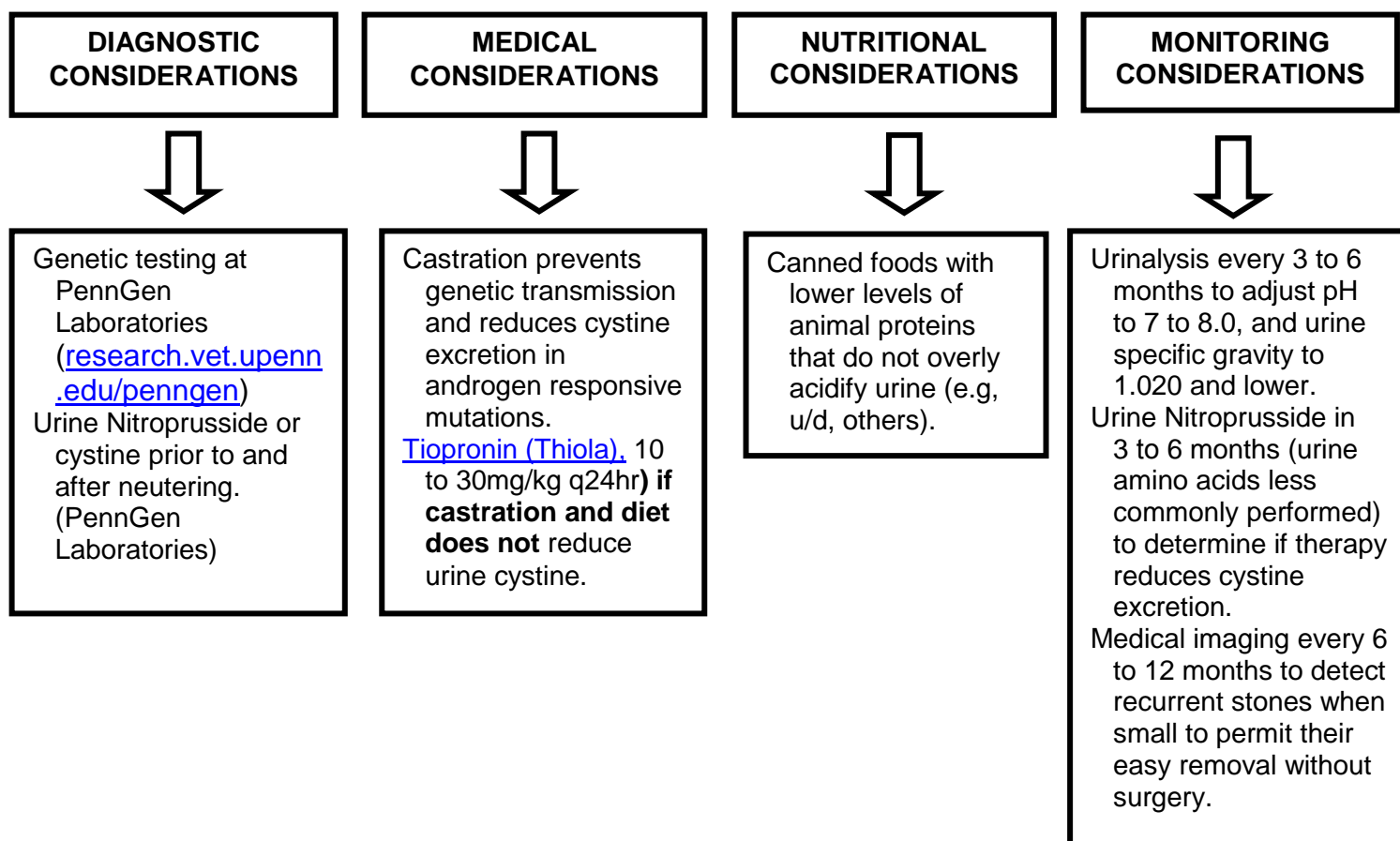
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CANINE CYSTINE

Cystine uroliths form because of inherited defects in renal tubular transporters of cystine. The transportation defect in dogs appears to be genetically heterogeneous (autosomal recessive-SLC3A1, autosomal dominant-SLC3A1 & SLC7A9, and sex linked/androgen responsive). In many dog breeds the mutation has not yet been determined.

PREVENTION



** Review manufacturer's therapeutic food literature to determine indications/contraindications. For pets with multiple health concerns, consult a veterinary nutritionist to select an optimal food.

In depth recommendations and references are available on our website: urolithcenter.org under the resources tab.

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Thiola 2017

CYSTINE UROLITH TESTING/MANAGEMENT OPTIONS

Neutering:

Genetic tests in some breeds are available to identify genetic carriers and affected dogs. Dogs with androgen-dependent cystinuria can be cured by medical (GnRH agonist implant for ~6months) and surgical castration. Testing the urine for cystine (nitroprusside test) **2–4 weeks** pre and **2–4 months** post neutering can be helpful to suggest a type I/II versus androgen-dependent cystinuria. Castration is recommended to potentially provide a cure, and to prevent the spread of this inborn error of metabolism.

Nutritional Considerations:

Dietary selection is an important part of preventative therapy for cystinuric dogs. Select low sodium canned foods with lower levels of animal proteins that do not overly acidify urine. [Consult a veterinary nutritionist](#) for options.

Pilot studies performed on cystinuric dogs at the University of Minnesota revealed a 20% to 25% reduction in 24-hour urine cystine excretion during consumption of Prescription Diet® u/d® canned diet compared to a canned maintenance diet

Thiola® (Tiopronin, 2-MPG)

Effective September 2014, Thiola is no longer distributed by Mission Pharmacal.

Thiola is available directly from the distributor Retrophin at:

Thiola Total Care Hub thiola.com/hub phone = 844-4-THIOLA (844-484-4652)

Tiopronin tablets are available through compounding pharmacies. Contact your preferred compounding pharmacy for availability. One pharmacy we have identified that offers compounded capsules and suspensions (confirmed availability: June 2016) Wedgewood Pharmacy wedgewoodpetrx.com 877-357-6613

Alternatives:

L-cystine methyl esters-

Studies in the mouse model have shown that these compounds are effective in disrupting cystine crystal growth. Future studies hope to show that efficacy and safety profiles are superior to current thiol-binding drugs.

Sahota, A: Novel Cystine Ester Mimics for the Treatment of Cystinuria-induced Urolithiasis in a Knockout Mouse Model: UROLOGY 84: 1249.e9e1249.e15, 2014

Cuprimine® D-Penicillamine-

D-penicillamine, also called dimethylcysteine, is a first-generation cysteine chelating drug. Although D-penicillamine is effective in reducing urine cystine concentrations, drug-related adverse events limit its use. Therefore, we have discontinued using D-Penicillamine for cystinuric dogs and cats.

Additional information regarding cystine urolithiasis:

vetmed.umn.edu/centers-programs/minnesota-urolith-center/recommendations

Osborne C, et al: Canine Cystine Urolithiasis: Causes, Detection, Dissolution, and Prevention: Small Animal Clinical Nutrition 5, Mark Morris Institute <http://bookstore.markmorrisinstitute.org/> (download at no cost)

Resources for cystinuria testing (urine nitroprusside/genetic testing):

[PennGen Laboratories](http://research.vet.upenn.edu/penngen) - <http://research.vet.upenn.edu/penngen>

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Visit our website: <http://www.cvm.umn.edu/depts/minnesotaurolithcenter>

CANINE CYSTINE UROLITHS

Cystinuria is an inherited defect in the transport of cystine. Cystine and several similar amino acids are normally reabsorbed by the renal tubules. Cystinuric dogs fail to reabsorb cystine from glomerular filtrate. The subsequently higher urine concentration of cystine is an important risk factor for urolith formation. As in humans, the transportation defect in dogs appears to be genetically heterogeneous¹.

Epidemiologic studies of uroliths submitted to the Minnesota Urolith Center indicate that male dogs (98%) are more commonly affected than females (2%). Common breeds affected include: Newfoundlands, Dachshunds, Mastiffs, Bassett Hounds, Staffordshire Bull Terriers, and Bulldogs. The mean age at time of urolith retrieval was 4.8 ± 2.5 years.²

Medical Considerations:

- Urine nitroprusside test is an effective screening test for cystinuria.
- Genetic tests for Newfoundlands and Labrador retrievers are available at the University of Pennsylvania (research.vet.upenn.edu/penngen) to identify genetic carriers and affected dogs.
- Cystinuria in some dogs may be androgen dependent. Considering neutering to reduce cystine excretion and prevent transmission of this genetic disease.

Nutritional Considerations:

- Avoid diets that promote urine acidification. Alkaluria promotes dissolution of cystine.
- High moisture foods (i.e. canned formulations) are more effective because increased water consumption is associated with decreased urine concentrations of calculogenic minerals.
- Limit excretion of amino acids such as cystine by feeding a low protein diet.
- Limit sodium intake. In cystinuric humans, dietary restriction of sodium reduced the urinary excretion of cystine.³
- Diets like Prescription Diet[®] u/d[®] canned diet fit these criteria.⁴

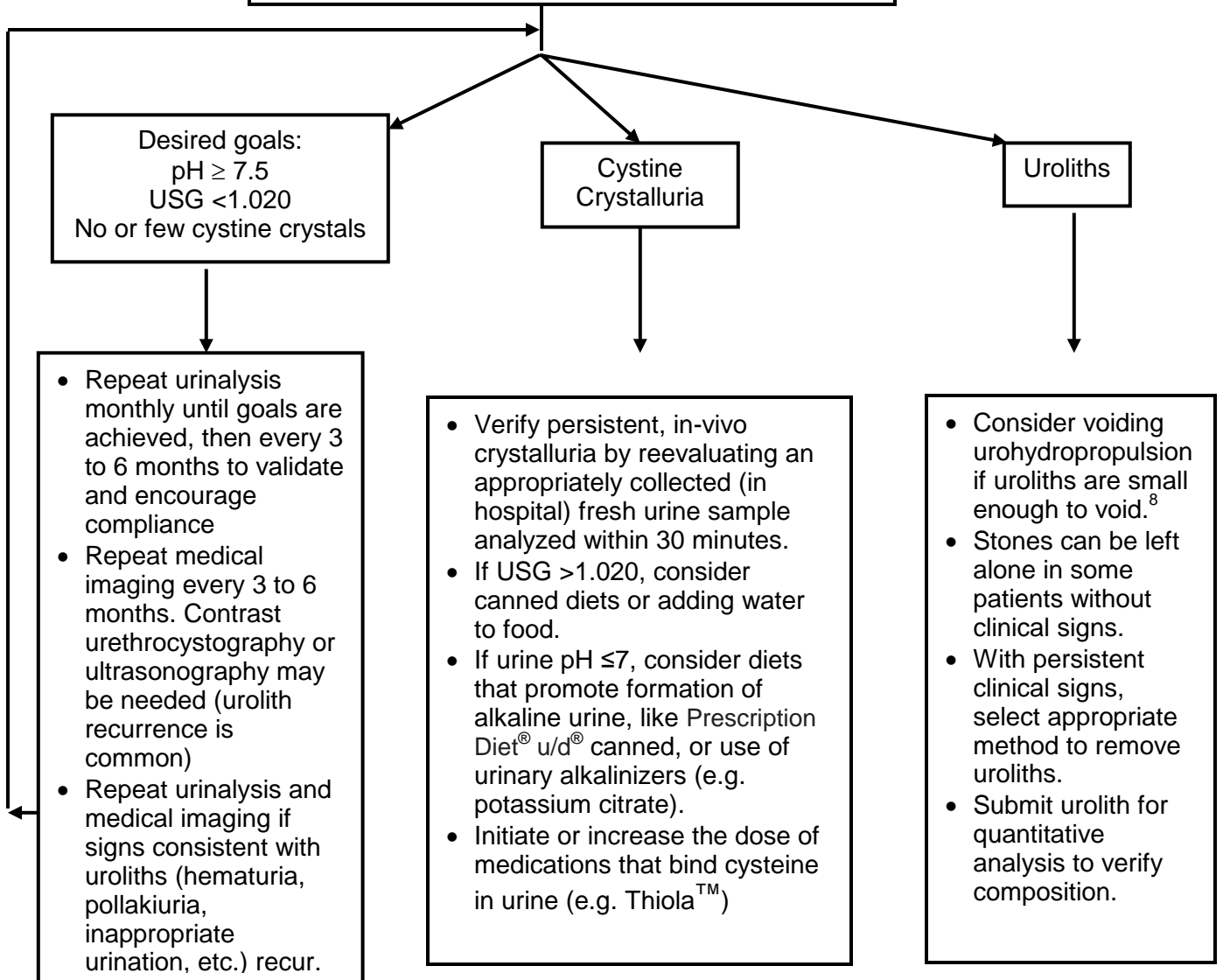
Pharmacological Considerations:

- For dissolution: In addition to dietary changes, administer n-(mercaptopyonyl)-glycine (2-MPG) (Thiola[™]) at an approximate dosage of 15mg/kg every 12 hours. Thiola[™] binds with cysteine molecules to form a complex that is more soluble in urine than cystine.
- Administration of alkalinizers may be necessary to maintain urine pH of ≥ 7.5 .
- For prevention: If diet alone is ineffective, consider addition of Thiola[™] at 10 to 30mg/kg/day to maintain a urine cystine concentration below 200mg/L.

Consider these facts:

- Experienced surgeons failed to remove all uroliths in 15% of dogs.^{5,6} Therefore, be diligent during surgery, and perform medical imaging immediately following surgery to verify complete urolith removal.
- Pilot studies performed on cystinuric dogs at the University of Minnesota revealed a 20% to 25% reduction in 24-hour urine cystine excretion during consumption of Prescription Diet[®] u/d[®] canned diet compared to a canned maintenance diet.²
- Cystine uroliths are highly recurrent.
- With increasing age, dogs appear to have a decrease in cystine urolith formation.^{7,2}
- Cystine uroliths are marginally radio-opaque. Contrast urethrocytography or ultrasonography may be needed to detect uroliths.

Managing Canine Cystine Urolith Prevention
Perform Urinalysis and Medical Imaging



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Further references:

- ¹Brons et. al. SLC3A1 and SLC7A9 Mutations in Autosomal Recessive or Dominant Canine Cystinuria: A New Classification System. JVIM.2013;27:1400
- ²Osborne CA, et al: Canine Cystine Urolithiasis: Cause, Detection, Treatment, and Prevention. In: Veterinary Clinics of North America, 1999,Vol. 29:1, 193-211
- ³Norman RW et al: Dietary restriction of sodium as a means of reducing urinary cystine. J Urol. 1990; 143:1193-1195
- ⁴www.hillsvet.com
- ⁵Lulich J. Incomplete removal of canine and feline urocytoliths by cystotomy. JVIM. 1993;7:124.
- ⁶Grant D. Frequency of incomplete urolith removal...in dogs. JAVMA. 2010;210:763
- ⁷Hoppe A, et al: Cystinuria in the Dog: Clinical Studies during 14 years of Medical Treatment. In J. Vet Intern Med 2001; 15:361-367
- ⁸Lulich J. Voiding urohydropropulsion a nonsurgical technique. Current Veterinary Therapy XII, SAP. 1995, p1003