**MINNESOTA UROLITH CENTER ★ University of Minnesota**

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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

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<th>DIAGNOSTIC CONSIDERATIONS</th>
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<th>NUTRITIONAL CONSIDERATIONS</th>
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<td>Genetic testing at PennGen Laboratories <a href="research.vet.upenn.edu/penngen">research.vet.upenn.edu/penngen</a></td>
<td>Castration prevents genetic transmission and reduces cystine excretion in androgen responsive mutations. <strong>Tiopronin (Thiola), 10 to 30mg/kg q24hr</strong> if castration and diet does not reduce urine cystine.</td>
<td>Canned foods with lower levels of animal proteins that do not overly acidify urine (e.g, u/d, others).</td>
<td>Urinalysis every 3 to 6 months to adjust pH to 7 to 8.0, and urine specific gravity to 1.020 and lower. Urine Nitroprusside in 3 – 6 months (urine amino acids less commonly performed) to determine if therapy reduces cystine excretion. Medical imaging every 6 to 12 months to detect recurrent stones when small to permit their easy removal without surgery.</td>
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<td>Urine Nitroprusside or cystine prior to and after neutering. (PennGen Laboratories)</td>
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** 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.
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) prior to 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.

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


Resources for cystinuria testing (urine nitroprusside/genetic testing):
PennGen Laboratories - http://research.vet.upenn.edu/penngen