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

** DIAGNOSTIC CONSIDERATIONS **

Genetic testing at PennGen Laboratories (research.vet.upenn.edu/penngen)

** MEDICAL CONSIDERATIONS **

Castration prevents genetic transmission and reduces cystine excretion in androgen responsive mutations. Tiopronin (Thiola), 10 to 30mg/kg q24hr) if castration and diet does not reduce urine cystine.

** NUTRITIONAL CONSIDERATIONS **

Canned foods with lower levels of animal proteins that do not overly acidify urine (e.g, u/d, others).

** MONITORING CONSIDERATIONS **

Urine Nitroprusside (urine amino acids less commonly performed) to determine if therapy reduces cystine excretion. Urinalysis every 3 to 6 months to adjust pH to 7 to 8.0, and urine specific gravity to 1.020 and lower. Medical imaging every 6 to 12 months to detect recurrent stones when small to permit their easy removal without surgery. Canned foods with lower levels of animal proteins that do not overly acidify urine (e.g, u/d, others).

** 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.
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 heterogeneous.1

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 additional to dietary changes, administer n-(mercaptoropionyl)-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 urothrocystography or ultrasonography may be needed to detect uroliths.
Managing Canine Cystine Urolith Prevention

Perform Urinalysis and Medical Imaging

Desired goals:
- pH ≥ 7.5
- USG < 1.020
- No or few cystine crystals

Cystine Crystalluria

- Verify persistent, in-vivo crystalluria by reevaluating an appropriately collected (in hospital) fresh urine sample analyzed within 30 minutes.
- If USG > 1.020, consider canned diets or adding water to food.
- If urine pH ≤ 7, consider diets that promote formation of alkaline urine, like Prescription Diet™ d/d™ canned, or use of urinary alkalinizers (e.g. potassium citrate).
- Initiate or increase the dose of medications that bind cysteine in urine (e.g. Thiola™)

Uroliths

- Consider voiding urohydropropulsion if uroliths are small enough to void.8
- Stones can be left alone in some patients without clinical signs.
- With persistent clinical signs, select appropriate method to remove uroliths.
- Submit urolith for quantitative analysis to verify composition.

• Repeat urinalysis monthly until goals are achieved, then every 3 to 6 months to validate and encourage compliance
• Repeat medical imaging every 3 to 6 months. Contrast urethrocystography or ultrasonography may be needed (urolith recurrence is common)
• Repeat urinalysis and medical imaging if signs consistent with uroliths (hematuria, pollakiuria, inappropriate urination, etc.) recur.

** 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.

Further references:
1. Brons et. al. SLC3A1 and SLC7A9 Mutations in Autosomal Recessive or Dominant Canine Cystinuria: A New Classification System. JVIM.2013.27:1400
4. www.hillsvet.com
6. Grant D. Frequency of incomplete urolith removal...in dogs. JAVMA. 2010;210:763
8. Lulich J. Voiding urohydropropulsion a nonsurgical technique. Current Veterinary Therapy XII, SAP. 1995, p1003

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