DCA Ultrasound Study 2005/2006

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It has long been understood that purebred Dalmatians possess an "inborn error of metabolism" with regard to purine proteins. This anomaly occurs in the liver and is considered a membrane transport defect which prevents complete conversion of uric acid to the water soluble product allantoin. To a lesser extent, the Dalmatian kidney is less efficient at resorbing uric acid than kidneys of other breeds. Therefore, abnormally high levels of uric acid are excreted in the urine (hyperuricosuria) of all purebred Dalmatians. Studies show uric acid excretion by Dalmatians is approximately ten times greater than other breeds. Since uric acid is relatively insoluble, crystallization of uric acid salts and/or calculus (stone) formation may occur in the urinary bladders of Dalmatians.[1-3] Clinical signs of dogs with urinary sediment or calculi may range from none to complete urethral obstruction and death if the obstruction is not relieved in a timely manner. It is not clear why some dogs with sediment or calculi obstruct and others do not.

For a general review of the Dalmatian's unique metabolism of purine proteins, including current recommendations concerning treatment and prevention of urinary stone formation in Dalmatians, please view the Dalmatian Club of America's Urinary Stone Study Group page on the DCA website (www.thedca.org/stones.html).

The defect in Dalmatians was shown to be inherited as an autosomal recessive trait by several investigators. Dr. Robert Schaible confirmed this with his early backcross work. All first generation progeny of the Dalmatian x pointer cross showed normal levels of uric acid. Recent research by Dr. Dannika Bannasch involving descendents of these backcross Dalmatians has narrowed the locus of this defective gene (huu) to a relatively small section of one chromosome.[4]

Dalmatians are referred to by scientists and breeders alike as stone-formers or non-stone-formers with the only evidence for this categorization being whether or not the dog has obstructed. Lacking in the literature is any information regarding the actual prevalence of urinary sediment and calculi in Dalmatians. The primary goal of this study was to document the prevalence of urinary bladder sediment and calculi in a population of Dalmatians attending DCA National Specialty shows in 2005 and 2006. Secondarily, we wanted to explore the influence of sex, urine pH and urine concentration (urine specific gravity) on the presence or absence of bladder debris as assessed by urinary bladder ultrasonography. Finally, owner input was requested in the form of a questionnaire to be completed for each dog screened. It should be noted that ultrasound evaluation of canine urinary bladders allows visualization of the contents of the bladder but not assessment of the mineral composition of any sediment or calculi present. Since the overwhelming majority of calculi from Dalmatians analyzed by all laboratories is urate in nature (see DCA references), we presume that the composition of sediment and calculi documented in this study follows the same trend.

Methods

Sample collection was conducted on 255 purebred Dalmatians at the DCA National Specialty show on May 1 and 2, 2005 and on 122 purebred Dalmatians at the DCA National Specialty show on April 30 and May 1, 2006. Both of these events were held in Ft. Mitchell, KY at the Drawbridge Inn. For each dog screened, owners were asked to complete a questionnaire recording sex, age, diet and supplements fed, medications, as well history of known urinary disease.

Owners collected first morning voided urine samples from 313 of the 377 dogs undergoing ultrasound evaluation. Trained volunteers analyzed samples to determine pH (to the nearest 0.5 unit) using ColorpHast strips from EMD, Gibbstown, NJ. Urine specific gravity (urine concentration) was determined using a Westover Model RHC-200 handheld veterinary refractometer manufactured in China. Accuracy was determined within 0.05 units. Susanne Hughes, DVM performed ultrasound evaluations with a Toshiba unit in 2005 and a GE Logiqbook in 2006. Both ultrasound units were provided by Sound Technologies, Inc. Results of urinary bladder ultrasound examinations were classified into four categories: no sediment observed, sediment less than 1mm (measured by calipers), calculi (stones) 1-3 mm, and calculi greater than 3 mm. Only one dog (2006 study) presented with a calculus greater than 3 mm. The individual had a complex history of multiple bladder surgeries and multiple stone types so was not included in statistical analyses in this study. Because the separation of classes based on sediment size was an arbitrary choice, analysis was carried out using both two classes (no sediment vs. any sediment present) and three classes (no sediment, sediment less than 1 mm and calculus greater than or equal to 1 mm).

Logistic regression was used to analyze the effect of the variables urine specific gravity (USG), pH and age on sediment class (either

two classes or three classes as described above). Contingency analysis was used to analyze the relationships between sediment class and sex and intact or neutered status. Differences in urine characteristics between groups were analyzed using one-way ANOVAs. Means are presented +/- 1 SE. Statistical analyses were carried out using JMP 5.0.1a software (SAS Institute, Cary, NC).

Results

Urine specific gravity (USG) exhibited the strongest relationship to the sediment class to which a dog belonged. When urinary bladder calculi were considered classified by presence and size into three classes, 189 dogs had no sediment, 84 had sediment less than 1 mm and 104 dogs had sediment/calculi greater than or equal to 1 mm. Dogs with sediment of any size present in their bladders had more concentrated urine, as indicated by a higher urine specific gravity (Fig. 1a; one-way ANOVA F=10.485, p<0.001). In contrast, there was no significant difference in urine pH in the classes with or without sediment (Fig. 1b; F=1.661, p=0.192). Dog age did not significantly differ across the three bladder sediment size classes (F=2.673, p=0.070).

Males and females did not differ in mean USG or urine pH, but more males than females had urinary sediment or calculi in their bladders. There were no significant differences between males and females in USG (males 1.039 +/- 0.0008, females 1.0311 +/- 0.0009; p=0.891, two-sided t-test). Mean urine pH was 6.38 +/- 0.03. Although males had a slightly higher urine pH (6.44 +/- 0.05) than females (6.32 +/- 0.05), the difference was not statistically significant (p=0.094; two-sided t-test). Mean age of dogs in the study was 3.9 +/- 0.2 years. Females in the study on average were older (4.5 +/- 0.3 yrs.) than males (3.4 +/-0.2 yrs.). Significantly more males than females had sediment or calculi in their bladders (Fig. 2). Only 25.4% of females had any measurable sediment present in their bladders, whereas 71.3% of males had sediment present (Fig. 2). Of the roughly ¼ of females with any sediment, 12.7% had sediment less than 1 mm, and 12.7% had calculi greater than or equal to 1 mm (Fig. 2). Of the roughly ¾ of males with any sediment, 30.7% had sediment less than 1 mm, and 40.6% had calculi greater than or equal to 1 mm (Fig. 2).

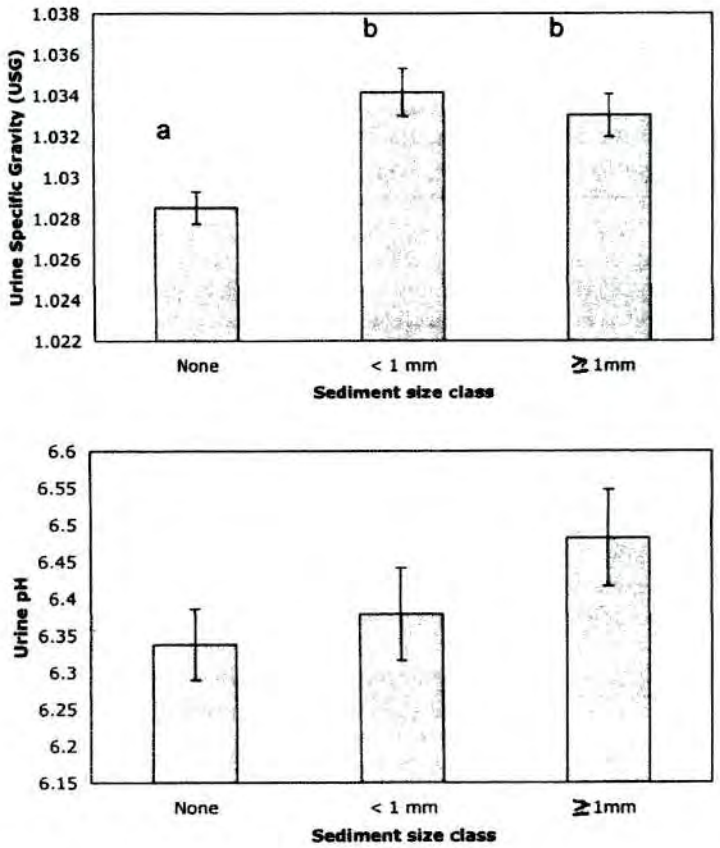
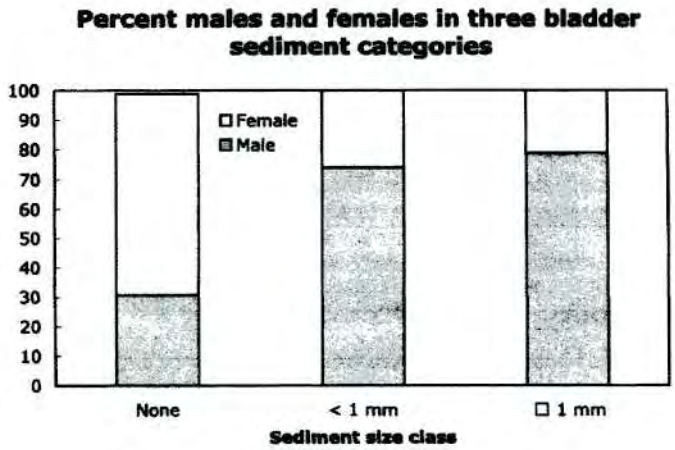


Figure 1a (upper) and 1b (lower). Mean (a) urine specific gravity (USG), (b) urine pH for dogs with bladder sediment in three size classes: no sediment, sediment < 1mm, and sediment ≥ 1mm. Letters above bars indicate statistically significant differences (α =0.05).



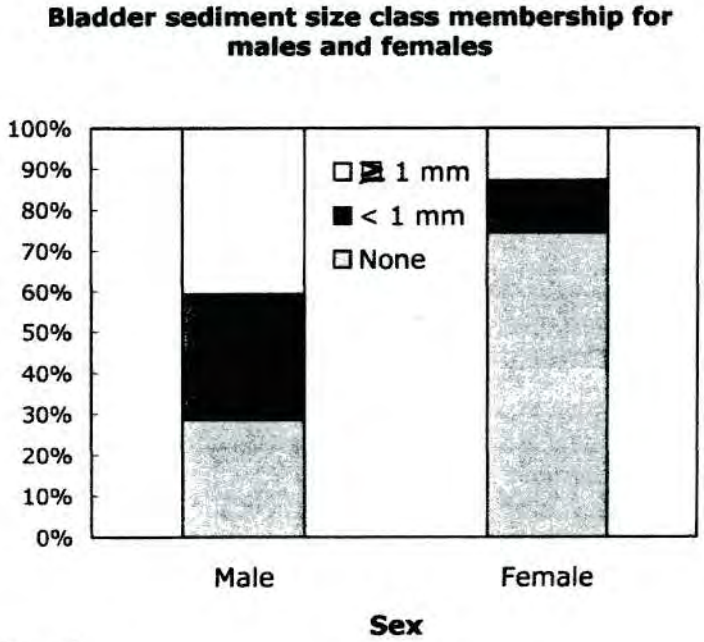


Figure 2.

Of the total 377 Dalmatians, 173 were females (115 intact, 58 neutered) and 202 were males (177 intact, 25 neutered) and 2 intact dogs did not have sex identified.

Of the 377 dogs, 17 dogs (4.5%) were being fed Hill's U/D diet, 9 dogs (2.4%) were taking the drug allopurinol, and 86 dogs (22.8%) were reported by owners as being fed primarily a raw food diet.

In 2006 four dogs identified as normal uric acid backcross Dalmatians were presented for ultrasound screening. Three were intact females and one was an intact male. All had bladders free of any sediment or calculi. Average USG was 1.042 and average pH was 6.25. None of these Dalmatian backcross dogs had a history of urinary crystal formation or urinary tract obstruction. These dogs were not included in the statistical analyses for this study of purebred Dalmatians.

Discussion

In this two season study, we attempted to determine how many, if any, Dalmatians participating in the DCA Ultrasound Clinics in 2005 and 2006 had sediment or calculi present in their urinary bladders as determined by ultrasonography. While there is no way to determine an actual prevalence in the general population of Dalmatians, one investigator reports 24.99% to 43.70% of male Dalmatians owned by respondents to a survey were clinically affected with urinary calculi.[6] To our knowledge, no studies have been published documenting results of ultrasound bladder studies in any group of Dalmatians. It is notable that a large majority of male Dalmatians in our study were found to have bladder sediment and/or calculi present. We are unable to predict which of these dogs are likely to obstruct, but it seems safe to conclude that all are at some risk relative to the population of all dogs without bladder debris.

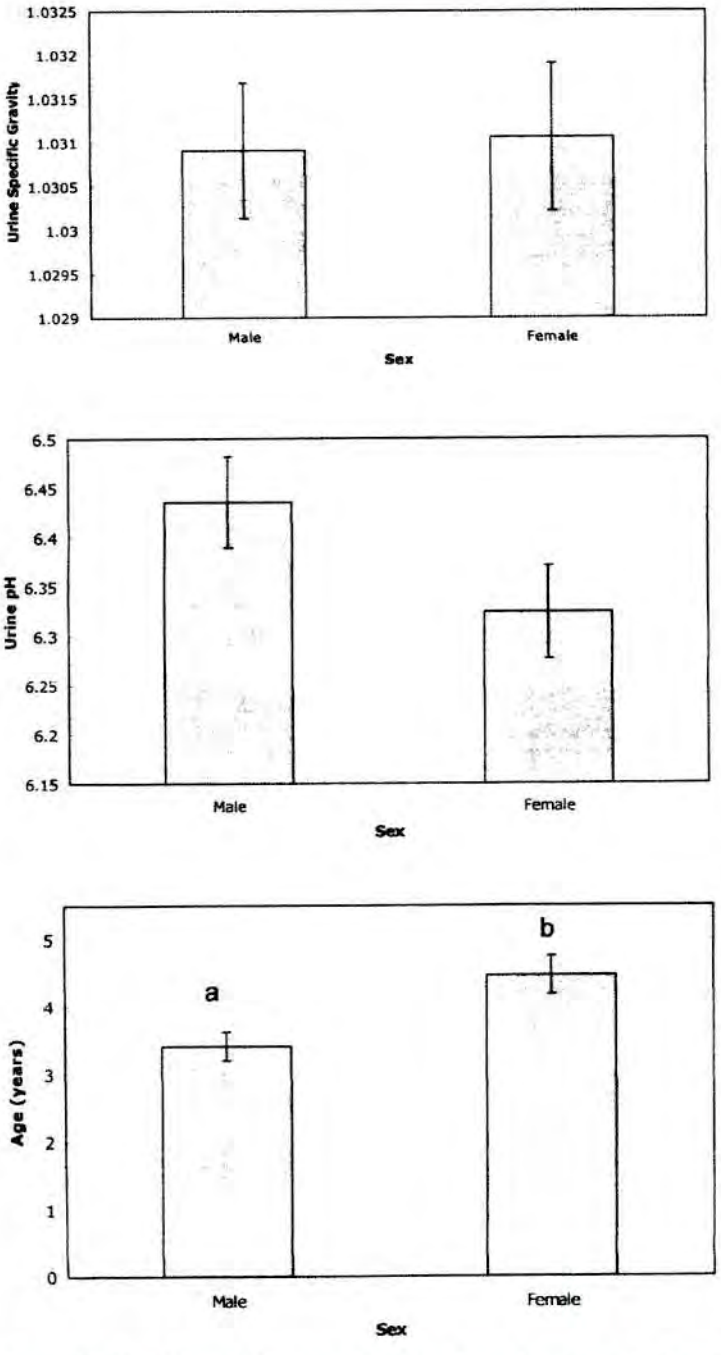


Figure 3(a, b, c). Mean USG, urine pH and age for males and females. Letters above bars indicate statistically significant differences (α =0.05).

It is important to note that data from the current study cannot be extrapolated to project a prevalence rate for the general population of Dalmatians. Dogs in this study were away from home, crated for longer periods of time than usual, possibly not drinking, eating or voiding on a normal schedule. These factors may have contributed to an artifactually higher prevalence than occurs in the general population of Dalmatians. It is not known how long it takes for sediment to flocculate into calculi 1 mm or greater in diameter, but it is likely not an overnight occurrence. Therefore, it is probable that at least for dogs having calculi measured to be 1 mm or larger, the bladder calculi were present prior to arrival at the shows where the clinics were held.

Clinically, problems associated with urate calculus formation affect male Dalmatians almost exclusively. These dogs present to veterinarians with recurrent urinary tract infections and/or urethral obstructions. Consistent with clinical observations and literature reports, we find many more males than females in this study have urinary bladder sediment and/or calculi. There are probably multiple factors responsible for this observation. Clearly anatomical differences are important. Females have a much shorter, wider and straighter urethra compared to males. Crystals and small calculi may pass easily out of the female urethra. As well as being much longer and narrower, the male urethra passes through a rigid tunnel shaped bony structure called the os penis. Calculi and even sediment can lodge along this narrow pathway, usually at the base of the os penis, obstructing urine flow and threatening the life of the dog. It is possible the difference observed in male and female bladder content may be fully explained by this anatomical difference. Supportive of this assertion is data showing that the percentage of all urolith types was significantly higher in male Dalmatians (69%) than females (29%).[1] It is currently not known if other variables contribute to this difference. Some speculate that the excretion of factors which inhibit uric acid crystal formation (Tamm Horsfall mucoproteins) is higher in female Dalmatians as compared with males.[1]

Potential risk factors influencing Dalmatian urate urolithiasis include diet (dry kibble, high purine content, acidifying diet and Vitamin C), urine (hyperuricosuria – common to all Dalmatians, aciduria, and highly concentrated urine); and being male.[2] Management of urate urolithiasis in Dalmatians includes dietary modification to control purine intake, increase urine pH, and lower urine concentration. By decreasing purine intake less uric acid is excreted. Prescription diets formulated to minimize urate urolith formation promote dilute neutral to alkaline urine (pH 7 – 7.5).[1] Unfortunately, these highly protein restricted diets may not support optimum body condition in all Dalmatians when fed long-term.

Monitoring protocols routinely describe frequent 'dip sticking' to determine urine pH as an important tool in managing or predicting a dog's propensity to form calculi.[5] In our study there was no significant correlation between presence or absence of urinary bladder sediment or calculi and urine pH. It must be noted that few dogs we screened were being fed a prescription diet and average urine pH was fairly low (6.38+/-0.03). In fact in recent years urologists have been placing more emphasis on lowering urine concentration to reduce sediment flocculation and subsequent calculus formation. From this study, it appears that this is certainly well-advised. Dogs having more concentrated urine were much more likely to have bladder sediment or calculi present. (Fig. 1a) Conversely, dilute urine (USG less than 1.020) was associated with 'clear' bladders or those with minimal sediment. Clearly more attention should be paid by owners and veterinarians to urine concentration when managing urate urolithiasis in Dalmatians. Recommendations should include increasing fluid content of the Dalmatian diet. This may mean feeding a canned diet, adding lots of water to dry diet or feeding a balanced homemade diet with plenty of water added.

Medical therapy in the form of allopurinol is sometimes prescribed to prevent conversion of xanthine to uric acid, thereby reducing urine uric acid excretion and calculus formation. As well, potassium citrate may be added to the diet to promote a more alkaline urine. Sodium bicarbonate is no longer recommended due to its propensity to cause metabolic imbalance.

Emergency treatment of obstructed Dalmatians can be very expensive and traumatic for both owner and patient. While current protocol for management and prevention of urate urolithiasis in Dalmatians is well described it is by no means simple or effective in every case. Recurrent urinary obstruction is quite common in male Dalmatians even when owners are diligently compliant with veterinary instructions. A large majority of male Dalmatians in this study (71.3%) had significant urinary bladder debris. We cannot accurately predict which dogs will obstruct and which will remain asymptomatic. It does not seem reasonable to suggest that all asymptomatic male Dalmatians be placed on strict urate urolith prevention protocols, including ultra low protein diets and medical therapy with allopurinol for life. The simple practice of adding plenty of water to the diet is proven clinically effective at reducing urine concentration, hence urine urate saturation, and should be done for all Dalmatians. In clinical practice, annual or biannual limited bladder ultrasound evaluations and urinalyses can provide helpful criteria for the veterinarian attempting to proactively manage urate urolithiasis in male Dalmatians.

Since all purebred Dalmatians are homozygous recessive for the *huu* gene responsible for hyperuricosuria, it is not possible for breeders to select for normal uric acid production in this gene pool. For breeders desiring to correct this defect, continued consideration of the Dalmatian x Pointer backcross project is certainly warranted.

References

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Living With Allergies and Your Dog

By Emily Hoover

1. Keep your dog out of your bedroom.
2. Keep your dog off the furniture.
3. Do not allow dog to lick your face or arms.
4. Wash hands after handling your dog.
5. If possible, provide crate in laundry room with air filter and/or vent (or away from bedroom).
6. Wash bedding weekly. (I use small amount of detergent and dry bleach with warm water.)
7. Vacuum floors, carpet and rugs often.
8. Change vacuum bag frequently.
9. During pollen season, use wipes or damp rag to wipe dog before he comes in the house.
10. Give dog weekly shower or bath. I use some of my conditioner to rinse dog to cut "doggie odor." This is a good time to clean ears, cut nails and check your dog over.
11. Vacuum in and under crate weekly.
12. Have your vent system cleaned every few years. You may also want to get an air filter that attaches to your furnace system. Be sure to check and change any disposable air filters frequently.
13. You may want to use borax (found in laundry isle) or baby powder on dog bedding to keep doggie odor down.
14. When traveling, shake or turn over bedding often. Take extra bedding and trash bag for dirty bedding.
15. If you have to – take allergy medicine or shots. I have taken Dripal, which you can get from your druggist. You may want to try Zicam Extreme Congestion Nasal Gel. I have found both very helpful. It is a small price to pay for the love of a good dog.

Living with allergies and your dog is not easy. But nothing worthwhile in life is ever easy, is it?