Letter to the Editor

The link between hyperuricosuria and urate urolithiasis

I am writing regarding the article “Validation of a urine test and characterization of the putative genetic mutation for hyperuricosuria in Bulldogs and Black Russian Terriers.”¹ In their conclusion, the authors state that “…the genetic mutation associated with hyperuricosuria, first identified in Dalmatians, also appears to cause hyperuricosuria in Bulldogs and BRTs, indicating that similar management strategies for urate urolithiasis can be used in these breeds.” The article ends with a final sentence: “This DNA test may also be used to genotype breeding dogs and aid breeders in reducing the incidence of hyperuricosuria and urate urolithiasis in susceptible breeds.”

Various experts, however, have suggested that hyperuricosuria is not the sole cause of urate urolithiasis. It has been pointed out, for instance, that “[t]he genetic mutation for hyperuricosuria in Bulldogs and Black Russian Terriers has the potential to decrease the development of urate urolithiasis in these breeds. Testing dogs of susceptible breeds not for hyperuricosuria but instead for the presence or absence of urate uroliths would appear to be mandatory to document the diagnosis of urate urolithiasis before any decrease in the prevalence of urate urolithiasis in these breeds could be determined. However, this requires following dogs well into adulthood, considering the onset of uroliths appears to be predominately between 1.5 and 6 years of age.

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The authors recognize that hyperuricosuria may not be the sole cause of urate urolithiasis. However, there is a vast body of literature beginning with the work of Dr. Keeler,² published in 1940, showing that hyperuricosuria is a cause of urinary calculi in Dalmatians and hyperuricosuria is clearly a predisposing factor. As stated in the article¹ cited by Mr. Weiss, “[h]yperuricosuria predisposes Dalmatians to urate urolithiasis.” In addition, although we could not locate the quote Mr. Weiss cited from Sorenson et al,³ the article does say that “[u]rate calculi have been recognized for many years by veterinarians and breeders as a serious and potentially life threatening complication of purine metabolic abnormalities in purebred Dalmatians.” Considering that hyperuricosuria is the manifestation of the purine metabolic abnormality in Dalmatians,⁴ this highlights the importance of hyperuricosuria for urate stone formation. These are not the only experts who identify hyperuricosuria as a major predisposing factor for urate urolithiasis in Dalmatians. Bärtges et al reports that “Dalmatians are predisposed to urate urolithiasis because of familial effects on uric acid metabolism”⁵ and that “Dalmatian dogs are predisposed to urate uroliths due to their unique metabolism of purines.”⁶ Low et al wrote that “Dalmatians have been reported to be at risk for development of uroliths because of a genetic defect that results in hyperuricosuria, which is caused by a defect in uric acid transport in the kidneys and liver.”

Because hyperuricosuria is required for the formation of urate stones (if urate is not present, it will not crystallize and form uroliths), decreasing the number of hyperuricosuric dogs in a breed will decrease the number of dogs that may form urate uroliths. Therefore, the authors believe that the DNA test may be used to “…genotype breeding dogs and aid breeders in reducing the incidence of hyperuricosuria and urate urolithiasis in susceptible breeds.”⁷

Additionally, management strategies in urate urolith–forming Dalmatians are aimed at reducing the amount of uric acid excreted in the urine and decreasing the urinary uric acid concentration through dilution, thus reducing the risk of stone formation.⁸ Because the hyperuricosuria phenotype is similar between Dalmatians, Bulldogs, and Black Russian Terriers, and the genetic cause for the hyperuricosuria is the same, these management strategies will likely benefit Bulldogs and Black Russian Terriers in the same manner that they benefit Dalmatians.

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The author responds:

We are happy to respond to Mr. Weiss’ letter regarding the study that was published in the August issue of AJVR.¹


