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M ost Dalmatian breeders and owners recognize the signs of urinary stones. Dogs suffering with stones have difficulty urinating. When they produce urine, it appears dark and thick like honey. Extreme dehydration is common.

About 10 percent of Dalmatians form stones even though all Dalmatians are genetically predisposed to the potentially fatal and painful condition. Researchers at the University of Tennessee College of Veterinary Medicine are trying to learn why some Dalmatians form stones and others do not. Their research, which is sponsored by the Dalmatian Club of America Foundation (DCAF), involves evaluating male sibling pairs in which one dog is a known stone former and the other is a known non-stone former.

"The original Dalmatian is considered a high uric acid (HUA) excreter, although now there are backcross Dalmatians known as low uric acid (LUA) excreters," explains Joseph Bartges, D.V.M., Ph.D., DACVIM, DACVN, professor of medicine and nutrition and the lead investigator. "If all HUA Dalmatians excrete high levels of uric acid in their urine, why don’t they all form urate stones? There must be something else that separates a urate-uroolith-forming Dalmatian from nonurate-uroolith-forming Dalmatians."

Genetic researchers identified a mutation in the SL C2A9 gene in Dalmatians that causes hyperuricosuria, or high uric acid levels, in 2009. Danika Bannasch, D.V.M., associate professor of veterinary genetics at the University of California, Davis, and Bob Schaible from Purdue University, analyzed urine and DNA samples from a backcrossed line of Dalmatians and a single Pointer.

While all Dalmatians are homozygous for the gene mutation, meaning they inherit two copies of the mutation, the backcross dogs were heterozygous, or had one normal copy of the gene. The backcross dogs produced normal levels of uric acid.

The SLC2A9 gene mutation results in an amino acid deficiency of a key protein involved in transporting uric acid to the liver. This contributes to increased excretion of uric acid and affects metabolism of uric acid into allantoin. While most mammals are able to metabolize purine compounds and produce water-soluble allantoin as a waste product, Dalmatians along with humans, great apes and English Bulldogs produce a different breakdown product, uric acid. Elevated uric acid levels can result in the production of uric acid salts or urate that crystallize and form stones.

Bartges’ research is investigating whether the gene mutation alone accounts for a predisposition to form uroliths. "We feel other factors are involved," he says. "Our genomewide comparison of littermates has identified several other genomic differences that may be involved in urolith formation." A Possible Kidney Association

Urinary stones can form at any age. If not treated immediately, stones can lead to urinary blockage. Males tend to obstruct because their urinary pathway passes over the os penis where stones can get lodged and cause an obstruction. Females rarely obstruct because there is no narrowing of the urinary pathway. The obstruction occurs when no urine is passing or when very little urine can pass.

One challenge hampering understanding Dalmatian stone disease is an inability to visualize stones on standard radiographs. This means it is not always clear which part of the urinary system — the bladder or kidneys — they originated. The majority of urinary stones are believed to occur in the bladder.

Stone disease may advance to kidney insufficiency and subsequent kidney failure. "Some people believe many Dalmatians form urate stones in their kidneys, which may be associated with recurrent stone formation, abdominal pain and possible kidney failure," Bartges explains. "Our study will evaluate how commonly urate stones form in the kidneys and the effectiveness of preventive measures for urate stones."

A hypothesis is that if urinary stones originate in the kidneys, kidney complications may be reversible by using effective anti-stone therapies that target the upper urinary system where the kidneys are located. The findings potentially will benefit Dalmatians with stone disease by helping to extend their lives and avoiding costly expenses for kidney disease.

Bartges has been involved with urolith research for 25 years, having written his doctoral dissertation on uric acid metabolism and urate stones. A component of this research involves collecting autopsy information from the kidneys and ureters of stone-forming Dalmatians. It is the first scientific project to gather autopsy data on Dalmatian stone disease in the kidneys and upper urinary system.

"There is concern about the number of Dalmatians diagnosed with kidney failure and/or kidney insufficiency," says Bartges. "Some cases of these life-threatening diseases may be caused by undetected stone formation in the kidneys and the upper urinary system."

The number of Dalmatians affected by urinary stones is not known. Some reports indicate as many as one-quarter

Dalmatian Owners May Contribute to Urolith Research

Owners of Dalmatians may help advance research under way at the University of Tennessee College of Veterinary Medicine to learn more about why some Dalmatians develop painful urinary stones while others do not. All Dalmatians are genetically predisposed to forming stones.

The research team is seeking 10 male sibling pairs in which one is a known stone former and the other is a known non-stone former. For information about participating in the research, please visit the Dalmatian Club of America website at www.thedeco.org or contact the lead investigator, Dr. Joseph Bartges, at jbartges@utk.edu, or veterinary nurse Amanda Callens at acallens@utk.edu.

Continued on page 2
Urinary Stone Formers
continued from page 1

to one-third of Dalmatians develop stones, while other sources suggest the disorder affects from 5 to 10 percent of the breed.

In their study, Bartges and his team have conducted a genomic evaluation of 20 male sibling pairs. They plan to evaluate 10 more pairs. In each pair, one dog was a known stone former and the other one was a known non-stone former. The study only included males because males are more predisposed than females and because they are more easily diagnosed. Additionally, it takes out gender-associated differences.

Their genomewide analysis, with help from a biostatistician, looked for associations between the two groups that would help to explain a genetic basis for stone formation. They evaluated 147,000 SNPs (single nucleotide polymorphisms) and found 874 that were different between the stone formers and the non-stone formers. Of these, 220 had less frequency, which gave them 654 possible associations.

“In assessing whether these had some importance, we were able to narrow it to seven strong candidate genes,” Bartges says. “Three of these were not involved in a coding region, and of these, two seemed to clinically/physiologically make sense.”

The two possible candidate genes identified are:

• SLC8A1 on chromosome 17
• CACNA1C on chromosome 27

“The SLC8A1 gene on chromosome 17 is most interesting,” he says. “Other SLC genes have been associated with high uric acid levels. Specifically, SLC2A4 variants may be responsible for high uric acid levels in Dalmatians, and SLC2A2 is involved with uric acid stone diseases in humans. In a study of human familial juvenile hyperuricemic nephropathy, the SLC2A4 region was identified. “To pursue this a bit further, we believe that we only need an additional 10 sibling pair samples or 20 non-sibling pair samples — male stone formers and male non-stone formers — to be able to determine the relevance of these findings.”

"Finding this marker would not only help Dalmatians and other breeds with urate stones, but also possibly humans,” says Meg Hennessey, DCAF president. “We hope to find additional male sibling pairs to continue this research.”

Tips on Living Free of Stone Obstruction

Dalmatians are prone to developing urinary stones due to an inability to convert uric acid to allantoin, a urinary excretion product of purine metabolism. Here are ways to reduce risk of stone obstruction in your Dalmatian.

• Make sure your dog receives plenty of water to help keep the urine dilute and prevent formation of stones. Try adding water to your dog’s food and teach puppies to enjoy ice cubes.

• Monitor your dog’s water intake and try to keep water bowls at several locations. Be sure to change water often.

• Allow your dog to go outside regularly and be sure to provide daily exercise. Stagnant urine in the bladder is more likely to form crystals and possibly stones.

• Because Dalmatians are unique in the way they metabolize purine-yielding foods, a low purine-yielding food is the healthiest.

• Pay close attention to whether your dog has trouble urinating, acts uncomfortable or urinates slowly. Take your dog to the veterinarian if you notice any abnormal behavior such as straining or difficulty urinating.

Dalmatians’ pH should be monitored periodically along with regular urinalysis. Owners can buy inexpensive test strips to test pH, acid or alkaline content in the urine. Ideally, a Dalmatian’s urine should be neutral with a pH of 7.0. Anything lower is acidic, and when the pH gets to 5.0 to 5.5, a dog is at risk for forming stones.

Urine should be tested the first thing in the morning after it has been in the bladder all night.

Since there is no test available to determine if an individual Dalmatian has a predisposition to develop urinary stones, Dalmatians owners are often encouraged to have a urinalysis several times a year. The test, which shows whether there are crystals or sediment in the urine, may help prevent obstruction.

Though much remains unknown about why some Dalmatians develop urinary stones and others do not, answers may be forthcoming from Bartges’ research. In the meantime, he advises breeders to not breed known stone formers. “If a known urolith former is part of a breeding program, it seems logical to discontinue using the dog,” he says.

“Increasing urine volume and perhaps feeding moderate protein-containing diets may also help.”

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Treating Stone Disease

Treatment for urinary stones usually begins with a medical dissolution procedure that involves feeding a low-purine, alkalining diet that induces dilute urine and administering the xanthine oxidase inhibitor, allopurinol. This results in less uric acid in the urine and promotes dissolution of the stones. The treatment is successful in about one-third of cases, in

which the uroliths decrease in size and number but do not fully dissolve. About one-half of cases result in uroliths small enough to be removed using endourological means. In the remaining one-third of cases, the uroliths increase in size and/or number usually due to xanthine formation. Allopurinol is a xanthine oxidase inhibitor that inhibits the enzyme, xanthine oxidase. This enzyme converts xanthine to uric acid. When the enzyme is inhibited, uric acid levels decrease; however, the trade-off is an increase in xanthine.

In additional to surgical removal, there are modern minimally invasive means of removing stones. Laser lithotripsy involves passing a scope through the urethra into the urinary bladder and using a laser to fragment the stones into smaller pieces that can be retrieved. Cystoscopic-assisted cystotomy is a technique similar to laparoscopy in which a veterinarian makes a small (usually <1 inch) incision in the body wall through which the urinary bladder is grasped and tackled. A small incision is made in the urinary bladder through which the scope is passed and the stones retrieved.

If a male dog has an obstruction, then the stones are flushed back into the urinary bladder, a procedure called retrograde hydropropulsion. If the stones cannot be pushed back into the urinary bladder or if stones keep recurring despite appropriate medical treatment, then a new opening can be made behind the bone in the penis so that obstruction does not occur, a procedure called scrotal urethrostomy.

Due to the Dalmatian’s inability to metabolize purine compounds, owners are urged to feed a diet with low purine-yielding proteins. “It helps to feed a purine-restricted, low-protein diet that increases urine volume, and then our studies show that pH appears the most effective with or without additional drug therapy using allopurinol,” Bartges says. “We found that administering 15 mg/kg of allopurinol every 12 hours was more effective decreasing urine pH than the often cited 10 mg/kg every eight hours.”

Adequate hydration is essential to avoid urinary stones. Dalmatians also should have ample opportunities to urinate. Acidic urine that sits in the bladder encourages the formation of urate stones.

A Dalmatian’s pH should be monitored periodically along with regular urinalysis. Owners can buy inexpensive test strips to test pH, acid or alkaline content in the urine. Ideally, a Dalmatian’s urine should be neutral with a pH of 7.0. Anything lower is acidic, and when the pH gets to 5.0 to 5.5, a dog is at risk for forming stones.

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Purina Pro Plan Introduces Canine Performance Training Treats

Dog trainers and handlers realize firsthand the importance of using food rewards to motivate dogs to perform at their best. Purina Pro Plan is launching Pro Plan brand Dog Snack Training Treats, a bite-sized, soft treat, to help trainers achieve top performance. Made with 80 percent chicken breast, Pro Plan Training Treats are highly palatable to help a dog stay focused on his game. Importantly, each treat is about 3 calories to help owners reward their dogs without overloading them with excess calories. Uniquely designed for training, Training Treats are easy to tear for quick rewards. Pro Plan Training Treats are formulated without corn, wheat, artificial colors or flavors. The treats will be available in June at pet specialty and farm supply stores. For more information, visit www.proplan.com or to talk to a pet nutrition consultant, call 800-PRO-PLAN or 800-776-7526, from 9 a.m. to 4 p.m. Central time Monday through Friday.

Purina-Sponsored Sporting Events*
June to August 2012

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‘Peyton’ Leads the Pro Plan Champions Cup Award Program

CH Wynmoo Champagne Supernova, a 5-year-old English Springer Spaniel campaigned by professional handler Robin Novack of Jackson, Mich., is leading the Pro Plan Champions Cup standings with 123 points earned through April 30.

The No. 4 dog in the country, “Peyton,” was bred by Billie and Charlie Kerfoot of Vinton, Va., Erin Kerfoot of Yakima, Wash., and Ruth Kirby of Earleton, Fla. He is owned by Beth Fink of Medina, Ohio, Celic Florence of Southern Shores, N.C., Erin Kerfoot, Ken Goodhue-McWilliams of Norco, Calif., and Delores Strong of Farmington, Mich.

The winner of 22 Bests in Show, Peyton recently outperformed more than 2,500 dogs to win the Atlanta Kennel Club Dog Show in Perry, Ga., and he captured a Sporting Group Three at the Westminster Kennel Club Dog Show. In 2011, Peyton won the English Springer Spaniel Field Trial Association National Specialty and Best of Breed at the AKC National Championship. In June 2011, he became the second dog in history to win back-to-back Bests of Breed at the Eastern English Springer Spaniel Club Specialties.

The yearlong Pro Plan Champions Cup award program is based on points tabulated from Bests in Show and Group placements at more than 200 Purina-sponsored all-breed dog shows in 2012. Three-year-old Black Cocker Spaniel GCH Casablancia’s Thrilling Seduction took top honors in last year’s program. This year’s winner will be announced in early 2013.

The Pro Plan Champions Cup winner will receive a $10,000 cash prize, an original oil painting by dog portrait artist Linda Draper and a keepsake Pro Plan Champions Cup trophy. A permanent Pro Plan Champions Cup is displayed at the Purina Event Center in Gray Summit, Mo., along with a plaque engraved with the winners’ names.

Cash prizes also will be awarded to the top-placing dogs as follows:

- Second place, $5,000
- Third place, $2,500
- Fourth place, $1,250

To view a tabulation of individual dog’s points and a listing of qualifying shows, please visit the Purina Pro Club website at www.purinaproclub.com.

GCH Wynmoo Champagne Supernova
English Springer Spaniel

GCH Mt. View’s Ripsnorter Silver Charm
German Wirehaired Pointer

GCH Szumerias Wildwood Silver Six Pence
Kuvasz

GCH Starline’s Chanel
Whippet

GCH Babheim’s Captain Crunch
German Shepherd Dog

GCH Marlex Classic Red Glare
Miniature Pinscher

GCH Banana Joe Van Tani Kazari
Affenpinscher

GCH Afterall Painting The Sky
Wire Fox Terrier

GCH Jaset’s Satisfaction
Standard Poodle

GCH Of Skyline Captain Hook
Skye Terrier

*Points earned through April 30, 2012