Dalmatian Urate Stone Forming Problem
An Independent Review of its Science

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"Dalmatian Stone Disease" and "Backcross Project" are words stirring a lot of conversation lately. We can all agree that Dalmatians have defects in protein metabolism and in basic urine formation that predispose the breed to urate stone disease. We can all agree that the diagnosis, treatment, prevention and eradication of these defects would be a good thing for our beloved breed. The purpose of this article is to pause for a moment in our national conversations and to look critically – scientifically – at the existing body of knowledge to figure out:

1. What we know,
2. What we think we know, and
3. What we don't know!

For background, DCAF President Eva Berg asked me (Spring/Summer 2006) as an independent scientist to review some new study findings and writings she kindly forwarded to me. With an open, unbiased, and non-conflicted mind, I eagerly set about to review the materials as a medical doctor, as a national peer review consultant experienced in the evaluation of scientific reports, and as a Dalmatian breeder.

As is true of most science, more questions came up than were answered. This prompted more reading, more thought, and finally resulted in a comprehensive ***Review***, which is planned to be made available on the DCA website. DCA President Dr. Charlie Garvin asked that this *Spotter* article be prepared as a summary of that ***Review*** for you.

Let's begin by recognizing that a large body of credible scientific evidence exists showing us that "Dalmatian Stone Disease" consists of at least three abnormalities that are found in the Dalmatian liver, kidneys and bladder:

1. Their livers don't completely metabolize purine-yielding proteins resulting in the production of too much uric acid,
2. Their kidneys don't properly excrete or absorb the increased uric acid, and
3. Their bladders can't always keep the increased uric acid in solution – hence crystals or stones may form.

What results from these three known abnormalities? One is that our cherished breed produces up to 20 times more uric acid per day (from 200 to 800 mg/day) than normal dogs (15 to 40 mg/day). That amount of uric acid sloshing around in the Dal bladder can precipitate out to form urate crystals, and those crystals can group together to form stones. It is very important to remember that despite the high level of urinary uric acid, the ***majority*** of Dalmatians do not seem to continue on into active stone disease. Only a ***minority*** of Dalmatians will actually progress into active stone disease with clinically detectable symptoms, and in the worst late-stage case will have a complete obstruction of the urinary stream by stones that can be life threatening.

Note that I very carefully used the words ***"majority"*** and ***"minority."*** Scientific evidence just does not exist permitting us to know how many Dalmatians per year develop symptoms of these breed defects, or how many U.S. Dals at any one moment in time have active stone disease. Why? Because we have no records or means to count up all of the Dals in the country, and then no way to count up the verifiable number of "normal" Dals versus "diseased" Dals. We just don't know what percentage of our Dals are affected – 10%, 20%, 30% – or whether more or less. Although we know that 100% of Dals have the defects in protein metabolism and in basic urine formation, no scientific evidence exists to estimate a credible, meaningful percentage of how many Dals shift from inactive disease into the full blown symptoms of active stone disease.

One thing is clear, though. The most common site for obstruction is at the urethra, and predominately in males. This makes scientific, biological and physiological sense because males, anatomically, have the os penis. This narrow tubular cartilage leading from the bladder to the outside world is a choke point where even small stones become trapped. Bitches do not have an os penis and they are at lesser risk, but still can form stones elsewhere in the female urinary tract (in the ureter or kidney itself).

Also, there appears to be a clear relationship with the overall state of hydration (fluid intake) of the Dalmatian and stone disease. Interestingly, Dr. J. Bartges in a recent DCAF-supported survey analysis identified a relationship between feeding dry kibble food and an increased likelihood of stone disease. While any survey study carries possible scientific criticism of its conclusions, it seems easy, common sense, and harmless to generously wet your Dalmatian's kibble food with the hope and likelihood that it, alone, can reduce Dalmatian stone disease. We know well that our Dals need ready access to water, water, water. One possible way to keep uric acid in solution is to see our Dalmatians drink as much water as we can get into them, and floating kibble in it seems simple enough!

What about testing for urinary uric acid in Dalmatians? There has been a lot of writing and controversy on this subject. The touted "gold standard" has been a laborious 24-hour collection of urine. The so-called "spot" sampling methods have been reported to be

unreliable. The definitive work on this by Dr. Bartges was conducted in normal female Beagles that produce 20 times ***less*** uric acid per day than our Dalmatians. While his report is a scientific masterpiece for Beagles, it has never been validated in Dalmatians by duplicating the research for their extreme ranges of abnormal urinary uric acid. Until the proper scientific study correlates with Dalmatians, we just will not know whether spot sampling is valid or not to estimate daily uric acid production in the Dalmatian.

Before I shift gears to the "Backcross Project" let me leave you by emphasizing one observation – a large number (the ***majority***) of Dalmatians producing from 200 to 800 mg of uric acid per day are not diagnosed with clinical stone disease. Why? Is all of this under some genetic control, or instead are there more significant influences from environmental factors (access to water, type of food, frequency of urinating, activity level etc.), or are there perhaps even other hormonal or other physiological influences. From a scientific perspective, it will probably be a combination of factors including genetic, environmental, and physiological all of which interact with liver-kidney-bladder dysfunctions to finally produce active stone disease. Fixing any one isolated part of the total problem will probably not be a single or predominate solution.

In 1973 Dr. Schaible conducted a single cross breeding of a Pointer to a Dalmatian with the purpose of introducing genetic material into the Dal hopefully to restore normal uric acid levels. Subsequent "backcross breeding" of the hybrid offspring to "pure" Dalmatians are presently in the 11th generation. It is important to know that only one breeding to a Pointer was involved; all others have been to Dalmatians.

The thinking is that the genetic defect follows a Mendelian recessive inheritance pattern. To understand this, remember your genetics of coat color in liver Dals which follows the same recessive pattern. For the uric acid defect, our Dals are [uu] (recessive). The Pointer is [UU] (dominant). The backcross produced [Uu] Dals. Since big U is dominant, the backcross Dals were theorized to produce normal canine levels of daily urinary uric acid. In any breeding of a backcross Dal to a non-backcrossed Dal, approximately 50% of the puppies will be [uu] and 50% will be [Uu].

To sort puppies at 5 to 7 weeks, urine is collected to spot test urinary uric acid to urinary creatinine ratios (UUA:UC). From limited reports on websites and in e-mails, there appears to be a 10-fold difference between "low" and "high" uric acid puppies, with a high variability (big range) of values for the "high" pups. According to basic research procedures, this methodology has not been independently scientifically validated (just as the testing in Beagles has not been confirmed in Dals, as noted above). However, a recent provocative study published by Doctors Safra, Schaible and Bannasch (2006) has correlated the "low" UUA:UC results with a specific genetic marker REN153PO3 located on chromosome CFAO3. Fantastic! Could it be that we are honing into the specific Dalmatian uric acid defect as one area in the canine genome coding for roughly 20 genes?

Nonetheless, ***caveat emptor*** (buyer beware)! Dr. Schaible in another publication links the genetic domain of the breed-specific uric acid abnormality to the T locus, that genetic area also controlling spotting or "ticking." Spot pattern is an extremely important type-specific matter for Dalmatians. Photographs of Backcross Dalmatians available on the Internet show some issues in spotting size, pattern and clarity. This appears to be a possible backcross "packaging" which each of us will have to judge for ourselves.

In closing I think that these are really exciting times for our beloved Dalmatians. Great strides are in the making to understand "Dalmatian Stone Disease." Given that there are at least three anatomical locales of the disease to correct – liver, kidneys, bladder – and adding to those the complex interplay between genetics and environment, one isolated solution will likely not be enough. We will probably need many. It is a good thing that our fancy and our leadership are so engaged in thought, controversy, and conversation about this. Let's try to adhere to fundamental basics of good science, and keep all options open for the betterment of the breed.

I would be happy to discuss the scientific ***Review*** (www.thedca.org) or this summary with you by e-mail (ibkmd@hotmail.com) or by regular mail.