

Responses to Questions From Those Who Are Opposed to AKC Registration for
Descendants of the Backcross Project.

Prepared by Denise Powell

Question 1. If the purpose for registering descendants of the backcross project is to improve the breed and to replace the mutant gene with the normal low uric acid gene, it would seem more appropriate to ask for registration of only those get that are homozygous for the normal gene, that is UU dogs. All offspring of these dogs then would have one normal allele.

Why have only 7 homozygous UU dogs been produced?

Why should we not restrict the registration to only UU dogs?

Why should we not delay registration until more such dogs have been bred and more evidence collected that there are no detrimental genes present?

Answer: There are a couple of reasons why few homozygous LUA Dalmatians (also called UU Dalmatians) have been produced so far. The only way to produce UU Dalmatians is by breeding an LUA Dalmatian to another LUA Dalmatian. Although the LUA Dalmatian breeding program began over 30 years ago, there has never been a time when there was a large, genetically diverse population of LUA Dalmatians from which to choose breeding pairs.

Even now, when the number of adult LUA Dalmatians is larger than it has ever been, they are all very closely related to each other. LUA Dalmatian breeders who do not want to produce inbred puppies, still do not have many choices from among the available LUA Dals. The only reason there are any suitable LUA breeding pairs at all is because breeders have made an effort not only to increase the number of LUA Dalmatians but to increase the genetic diversity by breeding to Dalmatians from many different lines.

Another thing to remember is that prior to the development of the DNA test for the normal SLC2A9 gene, LUA Dal breeders in the past had to wait until pups grew up and produced pups of their own to confirm which were homozygous (UU) and which were heterozygous (Uu). Thanks to Dr. Bannasch, LUA Dalmatian breeders know if there are any UUs in a litter before the pups are old enough to be placed.

Very few breeders have the resources or patience to grow out many dogs and do test breedings. LUA Dalmatian breeding entered a new era with the development of the DNA test. It is impossible to over emphasize the importance of Dr. Bannasch's contribution to the future of LUA Dalmatians.

When DNA tests become available, many people's first reaction is to focus exclusively on homozygous normals and overlook the value of heterozygous normals. That is why

Health and Welfare Advisory Committee included a warning about creating a population bottleneck or a popular sire effect. Restricting registration to only UU Dals (homozygous normal) would create the bottlenecks and popular sire effects that need to be avoided.

As tempting as it may be to rush the process of producing all LUA litters, it is important to avoid diminishing the genetic diversity of the gene pool. It is vital that the normal SLC2A9 gene be brought into the general population of Dalmatians through many individuals. To do this right, LUA Dalmatian breeders are going to have to accept getting some HUA pups in litters for many years to come. There are no quick fixes for genetic problems that are widespread in a breed. But every LUA pup that is born is one less Dalmatian at risk of forming urate stones.

The suggestion that registration be delayed reflects the fact that it is possible for different people to reach different conclusions even though they have access to the same data and even though they are motivated by the same desire to do what is best for the breed. On one hand we have LUA Dalmatian breeders and members of the Health and Welfare Advisory committee looking at the data and seeing minimal to nonexistent risk of LUA Dalmatians having any detrimental genes that do not come from their AKC Dalmatian ancestors. On the other hand, we have people who are concerned about a very remote possibility that the one Pointer passed on genetic defects that have remained undetected for 10 or more generations.

While it is proper to be cautious, it is important to temper caution with reason. Every breeding, whether of AKC or LUA Dalmatians, involves weighing the odds and making a decision about what is likely and what is unlikely to be produced. The chance that there are any unknown, detrimental Pointer genes carried by today's LUA Dalmatians is less than one in a thousand.

Question 2. The hallmark of good scientific research is careful, accurate and complete record keeping. Among scientists it is accepted that both results supporting the study hypothesis as well as results denying it will be carefully documented. Therefore, the following information should be made available about all descendants of the backcross project starting with the original 1973 hybrid:

- a. Total number of progeny of the Pointer/Dalmatian hybrid.
- b. What percentage of the LUA and the HUA dogs were ultrasounded to determine if they had bladder sediment or stones?
- c. How many of the get that are HUA have bladder sediment?
- d. How many of the get that are HUA have stones and or have obstructed?
- e. Are there any stone formers among the LUA dogs?
- f. Among both the LUA and HUA stone formers, what was the chemical analysis of the stones?
- g. How many of the stones were urate stones?

Answer. This question is based on a false assumption that vital records have not been kept and an unrealistic expectation that today's LUA Dalmatian breeders are conducting a formal research project.

It is important to understand that Dr. Schaible's backcross project began in 1973 and ended in 1981. Simply stated, Dr. Schaible's goal was to produce show quality Dalmatians that were not at risk of forming urate stones and that could be registered with the AKC. In 1980 Dr. Schaible presented his data to DCA and the AKC. In 1981, based on that data, the AKC registered 5th generation offspring of the backcross project as purebred Dalmatians.

Before Dr. Schaible began his project, researchers had already determined that :

- Dalmatians had a metabolic defect that caused them to have very high levels of uric acid in their urine.
- The defect was a recessive trait.
- It is impossible for urate stones to form in urine that is not supersaturated with uric acid.
- HUA dogs can be distinguished from LUA dogs by measuring the amount of uric acid in the urine.
- The well established protocol, known as backcrossing, can be used to transfer a trait from one breed line to another.

The fact that Dr Schaible is a geneticist made him aware of the research that had already been done. He based his breeding project on sound science. But Dr. Schaible was not conducting new research on urate stone disease in Dalmatians. He was not attempting to find the answer to the question of why urinary obstruction occurs in some HUA Dalmatians and not in others.

After the AKC registered the two 5th generation offspring from the backcross project, some DCA members were able to convince fellow club members that DCA should have nothing to do with continuing the of breeding of LUA Dalmatians. In the early 1980's, the club voted to end all further discussion of LUA Dalmatians. So how is it now, that DCA members feel they can demand that Dr. Schaible produce records for all the progeny produced in the decades when the club was completely disinterested in what he was doing? It is completely unreasonable to ask Dr. Schaible to go to the effort of pulling boxes of old records out of storage to provide information for people who seem determined to find fault with everything he has ever done?

In the years between the mid 1980s and 2005 Dr. Schaible made no secret of the fact that he continued to raise 1 or 2 litters a year. Other breeders also produced LUA litters, independent of Dr. Schaible. No one was keeping count of all the pups from all the litters produced by anyone who was breeding LUA Dalmatians. How many Dal breeders could easily come up with an accurate count of all the pups they had produced over 20 - 30 years, as well as those produced by others who got dogs from them along the way? More importantly, what real difference does it make if there were 30, 40 or 50 litters born between 1981 and 2005?

Once DCA made it known that the club had renewed its interested in LUA Dalmatians, every effort was made to make information available. The LUA Dalmatians website was

created. Statistics about every modern litter can be found on that site. Test results for many descendants of the backcross project are available on the OFA website. As soon as UC Davis announced that the DNA test was available, the LUA group contacted the OFA to create a new database for those test results and to grandfather in DNA test results that were done as a part of Dr Bannasch's research.

So, it is frustrating to hear people say that LUA Dalmatian breeders are not providing enough information or the right kind of information. LUA Dalmatian breeders are not conducting research. We are dog breeders who are breeding dogs. We keep the same kind of records on the dogs we produce that other breeders keep. When asked by researchers, LUA Dalmatian breeders provided DNA samples and urine samples. Those who were able participated in Dr. Hughes' ultrasound study.

None of the many scientists, on the AKC's Health and Welfare Advisory Committee or the genetics committee that reviewed the history of the backcross project before LUA Dalmatians were registered in Britain felt that it was necessary to do bladder ultrasounds on LUA Dals or their HUA littermates.

Question 3. I believe that we all agree that we really do not know what percentage of the general purebred Dalmatian population has stone disease. All of the studies probably suffer from "selection bias" because they are either self-reporting or studies of veterinary practice populations. The reason given for introducing the Pointer normal uric acid gene into the Dalmatian is the opinion that stone formation is a very significant problem in the purebred Dalmatian population. The DCA Study Group on Urinary Stones quotes Dr. Joseph Bartges survey in which he found 22.8% of Dalmatians with a history of stone disease. Therefore, one would expect that in backcross HUA population this number should be approximated.

How many of the HUA descendants of the backcross project have developed stones? Is it roughly 23%? If the number is not approximately that, how do you explain the variation from the expected number?

Answer. Stone formation has always been of concern to Dalmatian owners. It was a concern in 1973; it is a concern today. The 2001 DCA Health Survey placed urinary stones, along with deafness, epilepsy and skin problems at the top for "Diseases and Health-related Conditions Respondents Felt Are Most Critical to be Studied for Dalmatians." It was reported in that survey that the principal prescription medicine, other than heartworm preventatives, was allopurinol (10% of the respondents reported that their Dals were on allopurinol).

Based on Dr. Bartges's data and DCA's survey of Dalmatian owners, there can be little doubt that stone formation is a significant problem in the breed: preventive measures are only partly effective. That is not opinion; it is fact. We can quibble about the exact percentage of Dalmatians that receive veterinary treatment for stones, but there can be no argument about the significance of the problem.

The HUA backcross descendents are at the same risk of forming urate stones as any other dog with high levels of uric acid in their urine. All conscientious breeders provide new owners of HUA Dalmatians with detailed information about proper diet and management to reduce the risk of obstruction. Just as many AKC Dalmatian breeders can honestly say that very few of the Dals from their lines end up needing medical treatment for stones, LUA Dalmatians breeders count themselves lucky not to have gotten many phone calls from pet owners saying their Dals have obstructed.

The fact that few HUA backcross descendants have been treated for stones should not be taken to mean that they are not at risk of forming stones. The Dalmatians in Dr. Bartges' study were categorized by sex, diet and neutering status. He found significant differences in risk for each of these categories. A proper comparison of HUA backcross descendants would be to dogs in the Bartges study of the same sex, on a similar diet and that had been neutered after maturity. It is important to emphasize that careful management of HUA Dalmatians can reduce but not eliminate the risk that they will suffer from urinary obstruction.

Question 4. Dr. Susanne Hughes, in 2005 and 2006, ultrasounded 377 purebred Dalmatians. Out of this entire sample, only 1 dog had calculi larger than 3 mm. This dog apparently had an extensive history of multiple bladder surgeries and multiple stone types – not just urate stones. She found that 71.3% of the males and 25.4% of the females had sediment or calculi in their bladders. The only statistically valid correlation she identified for sediment formation was the specific gravity of the urine. The higher the specific gravity (the more concentrated the urine), the more likely sediment formation. The specific gravity of urine can be regulated by water intake. She suggested at the end of the paper, and I quote: “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.” (Spotter, Summer 2007, p. 91)

What reasons are there that we should resort to the drastic measure of introducing Pointer genes when there are clinically effective ways to reduce the risk of urate stone formation? Can we not wait to make sure that there are no negative consequences of the introduction of the Pointer genes?

The following answer was written by Dr. Susanne Hughes.

Urate stones tend to be smaller than other types of stones. In fact, obstruction is often the result of a concretion of sediment and/or tiny stones at the base of the os penis rather than one single stone. This is also why male Dals obstruct more often than dogs that form other stone types - urates are small enough to make it all the way down the urethra to the os while oxalate and struvite stones usually are too large to do that. So pointing out that the calculi I found were small in no way minimizes the potential for obstruction (as even you noted in the example you quoted). Yes, urologists now agree that the most significant parameter to monitor for managing stone formers is urine concentration (USG). As well urologists agree that despite all efforts to increase water consumption (often a difficult task), Dals still form calculi and sediment and some males obstruct. The fact is that as I

stated in the paper, not even the strictest protocol with 100% owner compliance will prevent stone formation in many male Dals. And finally how many more generations of dogs descended from the SINGLE breeding to ONE Pointer does any statistician, scientist or logical thinker need to determine that these dogs have no occult genetic disease?

Question 5. Dr. Susanne Hughes ultrasounded 377 purebred Dalmatians and found that a significant number had sediment or small calculi in their bladders. At this time, we do not know what the correlation is between sediment and stone formation. The assumption is that those with sediment are more likely to form stones. However, this is only an assumption.

A follow up study of these 377 Dalmatians would be extremely valuable to determine how many with sediment actually went on to have clinical symptoms or obstructed. Would the LUA registration proponents agree to waiting for the results of such a study?

The following answer was written by Dr. Susanne Hughes.

There is clear evidence in veterinary literature that sediment is a precursor to stone formation. Flocculation of sediment and crystals results in stone formation. This is a dynamic scenario and as we know, not all Dalmatians with sediment obstruct. That being said, note also that Dalmatians can obstruct with NO discrete stone as the offender, only a concretion of heavy sediment. It would be great to have a large study (of similar size as mine) that identified asymptomatic dogs at time 0, followed them over years to determine incidence of obstruction, however it will not be done- not feasible on many fronts: too expensive, unwieldy in scientific terms and more importantly we (scientists) already have clear evidence of frequent obstruction of male Dals in every population (private practice, referral practice and veterinary schools). No veterinary professional is questioning the fact that this is a serious health issue in this breed.

Questions 6. The American Pointer Club takes a Health Survey of breeders every 5 years. The most recent survey was in 2007. Epilepsy/seizure disorder was listed as #2 health issue in the Pointer. There is some epilepsy in the Dalmatian, but probably it is not as significant as that in the Pointer. We do not know what the inherited factors are for epilepsy, but most likely there is an inherited pre-disposition that is multifactorial.

Has there been a concerted effort to look for epilepsy in both the HUA and LUA get of the descendants of the backcross project? How many cases have been identified?

Answer. Among the descendants of the backcross project born since 2005, there has been one reported case of epilepsy/seizure disorder. A few cases were reported in those born in the decades before 2005. There have been no reports of epilepsy/seizures in multiple littermates.

All Dalmatian breeders face the same concerns about epilepsy/seizure disorder. While not considered to be the biggest problem in the breed, epilepsy/seizure disorder is common

enough to warrant a DCA Study Group for this condition. DCA has been involved with several projects on epilepsy/seizure disorder.

Any formal efforts to track epilepsy in descendants of the backcross project would have to be done in conjunction with tracking the condition among their AKC Dalmatian relatives. Genetic epilepsy/seizure disorder showing up in the current or future generations of the LUA Dalmatian population would most certainly have been inherited from the Dalmatians in the pedigree and not from the one Pointer who only shows up in the 10th generation and beyond.

Question 7. Deafness is strongly associated with white-coated animals. The Pointer is fundamentally white. The American Pointer Club does not require BAER testing for a CHIC number and therefore we do not have an adequate indication of the frequency of deafness in the Pointer breed. Deafness is another characteristic that the mode of inheritance is unknown. Most likely it is multifactorial.

How many of the HUA and LUA descendants of the backcross project have been BAER tested? How many are deaf and how many are unilateral hearing?

Answer. For the past several years, BAER results for LUA Dalmatian litters have been available on the LUA Dalmatian website www.luadalmatians.com and as well as in the OFA online database www.offa.org . Between 2005 and 2010 - 30 LUA litters were born with a total of 202 pups. 183 had bilateral hearing, 15 had unilateral hearing and 4 were bilaterally deaf.

LUA Dalmatian litters have been BAER tested ever since BAER testing became available. Prior to advent of BAER testing, Dr. Schaible did what other Dalmatian breeders did, he used home testing methods to determine if pups could hear and kept notes about hearing for each litter.

According to his notes, the one Pointer had a positive effect on the hearing in the first few generations. But as that Pointer moved farther back in the pedigree, hearing stats returned to what was more typical for Dalmatian litters.

It does not matter that we do not know the frequency of deafness for Pointers. There are no plans to breed to another Pointer. The one Pointer that was used is now so far back in the pedigrees of LUA Dals that he cannot be expected to have any influence on hearing stats of current LUA Dalmatian litters.

Question 8. Dr. Schaible in his original proposal linked the excretion of high uric acid to dermatitis which was quite prevalent in the Dalmatian in the 1970's. The coat of the purebred Dalmatian since then has been tremendously cleaned up and therefore probably is not due to uric acid levels. The American Pointer Club in its 2007 health issue survey found that skin allergies was a concern in the breed.

Is there any difference in the frequency and severity of skin allergies between the HUA and the LUA descendants of the backcross project?

Answer. It is true that Dr. Schaible originally thought that skin problems commonly seen in Dalmatians in the 1970s might be linked to high uric acid. But over time, he did not observe a significant difference in the skin and coats of LUA and HUA Dals in the litters he produced.

The Dalmatian Club of America's 2001 Health Survey report stated that 39% of the Dalmatians in the survey had skin problems ranging from hot spots to allergies. That may be an improvement from the 1970s. But it indicates that skin problems are still common in Dalmatians. If any Dalmatians from LUA litters have skin problems, they cannot be blamed on a single Pointer ancestor who is 10 generations or farther back in the pedigree.

At this point in time, no studies have been proposed to determine if LUA Dalmatians have more or less skin problems than HUA Dalmatians.

Question 9. Dogs have 78 chromosomes or 39 chromosome pairs. Each chromosome contains a certain number of genes. With the exception of crossover occurring, the genes on a given chromosome are inherited as a package. Therefore, the LUA Dalmatian (with the U gene) is likely to have on chromosome 3 several Pointer genes. In addition, the normal uric acid metabolism gene (SLC2A9) has been identified as being part of region that is estimated to contain 24 genes. At this time we do not know what those other genes might be. Therefore, the LUA dog is likely to have several other Pointer genes on its chromosome 3. Crossover is also likely to have occurred on the other 38 chromosomes. To what degree we do not know. The presence of recessive genes from the Pointer cannot be determined until a significant number of descendants of the backcross project are bred to each other. We had an incidence a couple of decades ago where a stud was imported from Britain. Only when granddaughters were being bred to grandsons did the presence of the gene blocking brown or black pigment production become evident. The product was lemon spotted Dalmatians. Once a recessive gene is introduced into the gene pool, it is extremely hard to breed it out.

The Dalmatian breed was developed over several centuries and today is one of the healthiest and most functional breeds. What other breed is expected to go 25 miles?

Is the risk of accidentally introducing unknown recessive Pointer genes worth it?

Answer. Concerns about unknown recessive traits were reasonable in the early years of the backcross project. But the one Pointer that was used is simply too far back in the pedigrees of today's LUA Dalmatians for there to be any real risk that his remote descendants carry unknown genetic defects inherited from him. We can say with confidence that only trace of that Pointer that remains in the genes of today's descendants are the normal SLC2A9 gene and some non-harmful genes that also reside on chromosome 3.

We know that there are no harmful recessive genes that come along with SLC2A9 because they would have shown up in litters where the Pointer appeared twice in their 10 generation pedigree. And they would certainly show up in any UU Dalmatian living today. The existence of even one UU Dalmatian that does not have “Pointer defects” is proof positive that there are no defective recessive Pointer genes contained in the region near the normal SLC2A9 gene. A UU Dalmatian has two copies of the normal SLC2A9 gene as well as two copies of whatever other genes are inherited as a package with SLC2A9. Since there are already several UU Dalmatians with no “Pointer defects” this concern can be put to rest.

Question 10. OFA records indicate that the Pointer has about twice the frequency of hip dysplasia as the Dalmatian. Other breeds have had relatively poor success in reducing the frequency of it. Since we do not know how it is inherited or how to breed it out, it would be a real shame to see the Dalmatian have an increased issue with it.

How many of the total HUA and LUA descendants of the backcross project have OFA good or excellent hips?

Answer. Again it must be emphasized that only one Pointer, named Ch Shardown’s Rapid Transit, not the entire Pointer breed was used to begin the LUA Dalmatian breeding program. By all accounts that one Pointer was a healthy dog that live a long healthy life. Seven of Rapid Transit’s full siblings were also AKC Champions. He came from the famed Shardown breed line of Leon C. Schriver who was honored by being elected to the American Pointer Club Hall of Fame. Mr. Schriver was noted for unsparingly culling known carriers of genetic defects. Hip dysplasia would not have been tolerated in the Shardown line.

Confidence in the genetic health of Ch Shardown’s Rapid Transit has increased as successive generations of healthy backcross Dalmatians were produced since that initial crossbreeding in 1973.

To date, there is no evidence of hip dysplasia in any of the descendants of the backcross project. A search of the OFA online database brings up records for 17 LUA Dalmatians that have hip certificates. Two other LUA Dals have outstanding PennHip scores. If any descendant of the backcross project is ever found to have hip dysplasia, one would have to search for the source of that defect from among their thousands of Dalmatian ancestors because 99.97% of their genes come from those Dals and not one Pointer that appears ten or more generations back in the pedigree.

The Pointer is so far removed from modern LUA Dalmatians that line breeding on him is no longer possible. Even if someone decided to breed only LUAs to LUAs, they could not produce Pointer traits that were bred out of the LUA Dalmatians decades ago. A dog cannot pass on genes that they themselves did not inherit.

