

## **Are We There Yet?** A Discussion on the Control of Genetic Diseases by Rene Sauser

You just received a call from someone who bought a pet puppy from you 5 years ago. Their dog has been diagnosed with Luxating Patellas (Slipping Stifles) and the vet is recommending surgery to the tune of \$1500. Luckily they are not angry with you and they are not demanding a replacement pet or compensation for their expenses. They just wanted you to know.

If you have been breeding for any length of time and have produced more than 50 puppies and most of those puppies are at least 8 years old, chances are you've had a call like this before. It is a statistical certainty. That is, unless you move often enough that your puppy buyers can't keep track of you, or you are a puppy mill and do not sell directly to the public. The average dog used by a "reputable" breeder carries at least 4 or more "defective" genes, genes which when paired with defective genes from another dog in the right combination, have the capability to manifest themselves as a health disorder in its offspring. With more than 100,000 genes in a dog, it is very difficult to isolate and eliminate the defective ones while retaining the ones we want.

Many breeders will say at this point "Oh no, not me, I do my part! I OFA the hips and stifles on my dogs and CERF their eyes and test their thyroids and check for Von Willebrand's Disease. My dogs are cleared!". And that's when the finger pointing (also known as "it must have been the stud dog's fault" syndrome) and back stabbing begins. Breeding can be every bit as competitive and cutthroat as campaigning a Special. Everyone wants to produce that next National winner. No one wants to find out what they really produced was a puppy with a genetic disorder. But, they especially don't want anyone else to find out about their "dirty little secret". So, they thank the pet owner for the information, hang up the phone, and breath a deep sigh of relief that none of the breeders they compete with know this pet owner. Breeders also have a tendency to not "go looking for trouble", they do not generally care to call puppy buyers from time to time over the years to see how the pets they have sold are fairing.

So, is it true, if we OFA and CERF, test thyroids, and run blood panels, are we home free? Are all of the genetic disorders that crop up in our breed solely due to those that don't do these things, the so-called disreputable breeders, the backyard breeders, and the puppy millers? The answer to both of these questions is a resounding NO!

In his book, *Control of Canine Genetic Diseases*, George A. Padgett, DVM explains that while OFAing, CERFing and testing for some conditions is certainly better than nothing, it is nowhere near enough. Worse yet, by teaching newcomers (future breeders) and puppy buyers that these are the things to look for in a reputable breeder, we may be doing ourselves more harm than good. One thing I've learned over the years is that when people are only told part of the story, often it is what they don't know that CAN hurt them.

In his book, Dr. Padgett attempts to arm breeders with the whole story. He admits that there is so much we don't know about canine genetic diseases, that we are just beginning to scratch the surface. Rather than getting into yet another tiresome discussion on Mendelian Theory, (he leaves that discussion to geneticists like Malcome B. Willis in *Genetics of the Dog*) he focuses on applying, in simple terms that breeders can understand, what we do know about modes of inheritance in selecting dogs for breeding. He also points out how much we don't know and why. The following table formulated from data presented in the appendix of Padgett's book represents known genetic disorders affecting the Keeshond which meet any or all of the following criteria:

- The disease has been reported as being genetic in the Keeshond
- The disease has been reported to be genetic in other breeds and has occurred in Keeshonden
- The disease has been reported to be genetic in other species (non-dog) and has occurred in Keeshonden
- The disease follows family lines, and it occurs in multiple generations of a given line, and has occurred in Keeshonden

System Affected	Disorder	Mode of Inheritance	Age of Onset of Disease
Cancer	Histocytosis	Undetermined	<= 7yr
Endocrine	Congenital Adrenal Hyperplasia-like Syndrome aka The Disease	Undetermined	<2yr
	Hyperadrenocorticism	Undetermined	<8yr
	Hypothyroidism	Undetermined	<2yr
Hematopoietic & Lymphatic	Von Willebrand's Disease	Incomplete Dominance	<1yr
Heart & Vascular	Mitral Valve Defect	Undetermined	<1yr
	Patent Ductus Arteriosus	Polygenic	birth
	Pulmonic Stenosis	Polygenic	<1yr
	Subaortic Stenosis	Polygenic	<1yr
	Tetralogy of Fallot	Polygenic	<3mo
	Ventricular Septal Defect	Polygenic	birth
Immune	Atopic Dermatitis	Undetermined	<1yr
Integumentary	Castration Responsive Dermatitis	Undetermined	<3yr
	Ehlers Danlos Syndrome (Cutaneous Asthenia, Dermatosparaxis)	Dominant	<10wk
	Growth Hormone Responsive Dermatitis	Undetermined	<2yr
	Umbilical Hernia	Recessive or Polygenic	<6mo
Liver-Pancreas	Diabetes Mellitus	Recessive	<3yr
Neurologic	Epilepsy type R	Recessive	>1yr
	Epilepsy type und	Undetermined	>1yr
Ocular	Cataracts	Undetermined	varies
	Central Progressive Retinal Atrophy (CPRA)	Undetermined	<2yr
	Ectopic Cilia (aberrant Cilia)	Undetermined	birth
	Glaucoma	Undetermined	<3yr
	Optic Nerve Hypoplasia	Undetermined	<3mo
	Progressive Retinal Atrophy (PRA)	Undetermined	varies
Skeletal	Hip Dysplasia	Polygenic	<2yr
	Luxation of the Patella	Polygenic	<1yr
	Osteochondritis Dissecans (OCD) - Fractured Coronoid Process	Polygenic	<1yr
	Osteochondritis Dissecans (OCD) - Shoulder Joint	Polygenic	<1yr
	Overshot	Undetermined	<1yr
	Undershot	Polygenic	<1yr
Urinary	Familial Kidney Disease	Undetermined	<8mo
	Renal Dysplasia	Undetermined	<1yr

One can quickly determine from this table that there is much we don't know about the mode of inheritance for many of the disorders known to affect our breed. Still others are polygenic in nature. Only one disorder is known to be Dominant in its mode of inheritance and a second disorder is known to be Incompletely Dominant. So, what does this mean?

First, only disorders known to be Dominant in their mode of inheritance can be blamed on a single parent dog. Therefore, only Ehlers Danlos Syndrome and Von Willebrand's Disease (VWD) could possibly be blamed on the stud dog or the brood bitch alone. In addition, VWD, being Incompletely Dominant, may be difficult to detect without testing both parents specifically for the disorder. Everything marked as having a Polygenic or Recessive mode of inheritance means both sides of the breeding program, the stud dog AND the brood bitch, contributed to the problem. Everything else marked as "undetermined" means we simply do not know enough about it to determine a mode of inheritance today. Keep in mind that those disorders which carry a Dominant mode of inheritance are the easiest to determine and the easiest to eliminate from a breeding program. Therefore, one must assume that all the disorders classified as "Undetermined" more than likely indicate involvement from both sides of the pedigree. So all you breeders who repeatedly choose to blame someone else's line, look to your own line because you certainly had a part in it.

But why do we know so little about the mode of inheritance for so many of these disorders? Why do we even continue to have occurrences of Hip Dysplasia, Patellar Subluxation and Epilepsy? Here is where not knowing the whole story comes into play.

Dr. Padgett explains the difference between Open Registries and Closed Registries. The Orthopedic Foundation for Animals (OFA) and the Canine Eye Registry Foundation (CERF) are both examples of Closed Registries. A Closed Registry only assigns registration numbers to animals deemed to be phenotypically normal for the specific disorders for which the animal has been examined. Phenotype describes the things we can see or test for, whereas Genotype describes the actual genetic makeup of the animal. A dog can appear normal, but may still be carrying a gene for something we don't want. A dog may test clear for a particular disorder yet be carrying many of the genes which can contribute to that very same disorder occurring in its offspring.

OFA concerns itself specifically with orthopedic function. OFA registers phenotypically normal hips, elbows, patellae, shoulders and hocks. When a dog is determined to be "phenotypically" normal for hips, the OFA is saying that in radiographs of the hip joints, the animal does not display significant symptoms of this disorder. OFA evaluates the hips at 2 years of age or older. They have 3 grades of hips that fall in the phenotypically "normal" range: excellent, fair and good. They have 4 grades of hips that fall into the phenotypically "affected" range: borderline, mild, moderate and severely affected. Only the grades in the normal range will receive an OFA certification. However, and this is important, just because a dog has hips which meet the OFA's criteria for a phenotypically normal rating, that does not mean that dog does not carry some of the genes which can contribute to hip dysplasia if used for breeding. OFA examines radiographs to determine if the animal is affected. That animal may not be affected, but genotypically that animal can be a carrier. People, breeders and pet owners alike, need to understand this distinction. Just because the dam and the sire both have OFA numbers, that does not mean one of their offspring cannot have hip dysplasia.

As a side note, I often hear breeders say that a particular dog produced of their breeding does not have genetically inherited hip dysplasia, that the environment caused it. This is a very misinformed statement. A dog can not get hip dysplasia unless that dog is genetically pre-determined to have the capability to get hip dysplasia. Environment can contribute to clinical presentation of this disorder, only after the dog has the genes necessary for the defect to present. Again, just because neither parent has hip dysplasia does not mean the parents cannot produce the genetic combination in their offspring for them to have it. Only a very ignorant or unethical breeder would blame his/her problems on the environment and continue to breed without assessing the part genetics may have played in the problem.

Because the OFA is a Closed Registry, it only divulges information on those things found to be normal. It does not divulge any information on those things found to be affected. If a dog has normal hips and diseased patellas, the dog will receive an OFA number for the hips, but the OFA will not disclose the abnormal elbows or even indicate whether or not the elbows have been examined. So, just because a dog has an OFA number showing excellent hips, one should not assume that the dog is free of any other structural abnormalities. That is the whole story with OFA.

CERF also is a Closed Registry. CERF deals solely with ocular disorders. Dr. Padgett states, CERF will not issue a number to any dog that has any eye abnormality – be it PRA, cataracts, corneal dystrophy or any other ocular abnormality – “that seriously interferes with the dog’s normal functions”. Dogs with minor abnormalities that are not known to progress and that do not interfere with function may be certified. In the table you will see that the mode of inheritance has not been determined for any of the eye disorders known to affect Keeshonds. Just because a dog has a CERF number does not mean that dog does not carry the defective genes which could contribute to a problem. It only means that at the time of examination, the CERF felt that the dog had no progressive eye disorders or disorders serious enough to keep the dog from functioning normally. Also, people need to be aware that CERF certification is only good for one year. Just because a dog received CERF certification last year, it does not mean the dog would pass certification again this year. Notice for Cataracts and PRA, both of these disorders may vary as to age of onset. A dog may actually carry the genetic makeup required to eventually become affected but that may not be determined until well after the dog has been certified and been used for breeding.

So, as we can see, it is easy for people to derive a false sense of security in the certifications provided by Closed Registries. Let’s not fool ourselves, and let’s not fool our puppy buying public. More and more we see puppy buyers being educated to buy from a reputable breeder, because reputable breeders test for all known genetic disorders in the breed to certify their breeding stock is free of all known problems. The pet owner sees this as a health “guarantee”. Imagine their surprise when five years down the road their beloved pet is diagnosed with Patellar Subluxation. This is because pet buyers are not being told the whole story or adequately educated in the complexities of genetics.

The reality is, we don’t know enough about the mode of inheritance on the majority of genetic disorders affecting our breed to guarantee there will never be a problem in any puppy we produce. But, because we insist on believing that to be reputable breeders we must be able to offer such a guarantee, we try. The downside to this is that when reality finally bites us, we try to hide the awful truth. We don’t discuss our problems publicly, we point fingers at everyone else, we keep our skeletons in the closet, we avoid checking in with our puppy buyers. This is entirely counterproductive to what we, as breeders strive for, healthy dogs.

So, how do we get out of this mess? How do we take the steps necessary to eliminate disorders in our breed? How do we finally reach a point where we can say honestly, we produce only healthy dogs?

Dr. Padgett recommends Open Registries. An Open Registry records dogs which exhibit genetic disorders and makes that information available to breeders. Sounds wonderful in theory, but in reality, are we really ready to come out of the closet with our problems? Imagine being totally honest with a puppy buyer and saying to them, “Well, there are at least 33 disorders known to be genetically inherited in Keeshonden. I have performed numerous tests on my breeding stock, but because we don’t know everything there is to know about it, I can not guarantee you that the puppy you buy from me and fall in love with won’t later be diagnosed with PRA and go blind.”. Already I hear the car door slamming and rubber burning down my driveway as they head for the nearest “reputable” breeder, the one that offers a so-called “health guarantee for life”. Then they tell that other breeder that I have PRA in my line. A few hours later I get a call from a breeder in Canada that has decided to use a local stud on her bitch rather than my National winning Special she had originally intended to use... Hmmmm, I wonder why ... news travels fast via e-mail. On the bright side, I’d have plenty of spare time for a new hobby, maybe hairdressing.

So, how did the Cairn Terrier Club of America, the Poodle Club of America, the West Highland White Terrier Club of America, the Newfoundland Club of America, the Bernese Mountain Dog Club of America and the Great Pyrenees Club of America all manage to participate in Open Registries and actually benefit from doing so? The Westie people have formed their own registry but the rest of these clubs work with the Institute for Genetic Disease Control at UC Davis (GDC). The GDC has both an Open Disease Registry and a research registry. When enough data is gathered on dogs for a specific disorder in the research registry to draw conclusions about the mode of inheritance for that breed, the data is moved to the Open Registry and all information is made available to breeders.

These various clubs discovered that the first step towards solving a problem, is to admit you have a problem, and be willing to share whatever information you have on your problem with an open registry in the hope that one day they will have enough data to determine the mode of inheritance. Until there is enough data available on a breed population, we will never be able to determine the mode of inheritance for most of the genetic disorders prevalent in the breed. Until we are willing to openly discuss these problems, admit they exist and that we all have them in our lines to one degree or another without pointing fingers, we will never have enough information to make informed decisions in our breeding program. If we don't know how a particular problem is passed on, how can we eliminate it from our breed? We can't, and it would be unethical to tell our puppy buyers otherwise.

Dr. Padgett recommends breed clubs and their members initiate a program and lists the following items a breed club should do to enhance the ability of club members and other breeders to control genetic diseases:

1. **Generate a list of genetic defects occurring in the breed by surveying members and owners.** This list should be made available to members and breeders and the mode of inheritance, if known, for each trait should be listed.
2. **Form committees to assess the impact of each trait on the breed.** Obviously some genetic diseases carry a more significant impact to the dogs and their owners than others. An undershot bite, for instance, is not going to cause as much harm as PRA. Therefore, when choosing to breed dogs which may potentially carry a particular gene or set of genes for a genetic defect, obviously some risk is more acceptable in some disorders than in others. Remember that the average Keeshond carries at least 4 genes which could contribute to a genetic defect, we need to try to identify which genes that dog carries to determine if he/she should be bred and to whom in order to minimize risk. There are no "clean" dogs and there never will be, so the best we can do is minimize the risk, but we cannot do that if we don't know what we have.
3. **Advocate the registration of dogs and bitches affected with genetic defects as well as those believed to be carriers (dogs and bitches which have produced affected offspring or that are littermates of affected dogs) in an Open Registry.** To be effective, breeders will need to keep track of all offspring produced, not just the ones they keep. Breeders will have to do a better job of keeping in touch with puppy buyers to track the progress of offspring and to become aware of any genetic disorders which manifest in later years.
4. **Advocate the registration of dogs and bitches proven to be free of the genes for each undesirable genetic condition.** This will allow breeders with known carriers to locate potential mates which do not carry genes for that problem and thereby minimize risk of producing that problem.
5. **Develop lists of dogs known to be affected with, or that carry genes for, a given trait that are available for test matings and make that list freely available to breeders.** Here it is important to understand the purpose of test mating. No one is advocating production of genetically diseased animals. The purpose of a test mating would be to mate a suspected dog/bitch carrier with a known carrier to determine whether or not the suspected dog/bitch is indeed a carrier of a specific defect. In entering into test mating, one should be resolved to the fact that any offspring produced in a test mating are potentially carriers. All offspring should be treated as potential carriers. Any affected or carrier offspring resulting from test mating that is placed requires that the prospective owner be thoroughly briefed on the risks and implications regarding the particular genetic defect the puppy they are purchasing has or may have. All offspring need to be tracked to determine if any become affected thereby proving the suspected carrier to be a carrier.
6. **Determine which defects should be attacked on a breed-wide basis.** Those which are most damaging to breed temperament or which are most widespread or carry the largest impact on breeders and pet owners need to be addressed more strenuously than those which are determined to be less significant.
7. **Develop a brochure discussing the diseases that occur in the breed, giving clinical signs, methods of diagnosis – including special equipment required, age of onset, mode of inheritance and potential treatments – and prognosis.** This brochure should be made available to every club member, breeder and pet owner.
8. **Develop a brochure discussing the rationale of the various systems that can be used to control genetic disease and how to handle carriers and potential carriers of the various traits.** Dr. Padgett's book addresses various methods for this.

9. **Most importantly, strongly support those breeders and owners with the honesty, courage and foresight to openly register dogs affected with genetic disease, because there is no hope for control without knowledge.** Breed clubs should clearly state that the ethical course is to openly discuss dogs with defects or those that produce defects when selling a show dog, breeding prospect or stud service. The breed club should use all the peer pressure at their command to support open registration if their goal as a breed club is to bring their dogs as close to perfection as possible as stated in the club's constitution.

The last item is very important. If breed clubs make open registry participation a very ethical, very positive thing for breeders to do, eventually control of canine genetic diseases in our breed will become possible. If those breeders who participate willingly and honestly are rewarded by the breed club through elevation to a "Supremely Responsible and Ethical Breeders" list, something everyone would wish to aspire to, there could be hope that one day genetic diseases in Keeshonden would be very rare indeed. This is not something that will happen over night, maybe not even in my lifetime. But through education and awareness and through support from breed clubs and breeders, it is a realizable goal. Pet owners and the public also need to be educated on the fact that lifetime health guarantees are unreasonable expectations, but that breeders who actively participate in open registries are doing the best possible job of identifying problems in their lines and taking steps to systematically eliminate those problems. Pet owners should be encouraged to buy from these breeders above all other sources. Puppy buyers will need to be encouraged to report genetic diseases to their breeders, and breeders will need to tell puppy buyers they will be calling on them from time to time to see how their pets are doing. Many of the previously mentioned breed clubs participating actively in Open Registries today have already made a significant impact on the control of genetic disease in their breed.

Isn't it time we got started? Wouldn't we all sleep better if we could tell our puppy buyers that yes, there are problems, but I'm doing my part to eliminate them and yes, I do want to know if your puppy ever becomes affected. Wouldn't it be nice if we all could be open and honest about our problems and no longer live in fear of those phone calls and the repercussions when other breeders hear about them? Let me know what you think, are we ready for Open Registries in our breed? Are we there yet?

Note: *Control of Canine Genetic Diseases* by George A. Padgett, DVM, Professor of Pathology at Michigan State University is an outstanding text which every breeder, and those considering breeding should own. Published in 1998, this 256 page text provides much valuable information in pedigree analysis, record keeping and tabulated data a breeder can use to approach breeding from an informed standpoint and make progress towards eliminating genetic disease. Dr. Padgett's text is geared towards individuals interested in becoming responsible, ethical dog breeders and not just "people who mate dogs". The book is available through <http://www.amazon.com> for \$19.57.