

Progressive Retinal Atrophy

PRA and the Löwchen

In 2003, Cdn Ch Wildhearts Heaven Forbid had her initial CERF exam. Always a stunning puppy, she had matured into a very typey Löwchen and it was time to involve her in a breeding program. I can still remember the shock I felt when Nadine, her co-owner called to say the exam showed her to be PRA positive and in quite an advanced stage. A second test was done and the results were the same - positive for PRA. 'Java' was immediately spayed and now lives with her sister in a great home but as her sight continues to fail, there will be challenges and for this reason alone, research must be done to ensure other Löwchen and their owners do not have to experience this preventable condition.

Since Java's diagnosis, I have spent many hours learning about PRA and I am now ready to share this information with others.

Progressive retinal atrophy, or PRA as it is frequently termed, is a long recognized, hereditary, blinding disorder. The first modern description of this problem was in Gordon Setters in Europe, in the early years of the twentieth century, but since then PRA has been recognized in most purebred dogs. PRA is a disease of the retina. This tissue, located inside the back of the eye, contains specialized cells called photoreceptors that absorb the light focused on them by the eye's lens, and converts that light, through a series of chemical reactions into electrical nerve signals. The nerve signals from the retina are passed by the optic nerve to the brain where they are perceived as vision. The retinal photoreceptors are specialized into rods, for vision in dim light (night vision), and cones for vision in bright light (day and color vision). PRA usually affects the rods initially, and then cones in later stages of the disease. In human families the diseases equivalent to PRA (in dogs) are termed retinitis pigmentosa.

In all canine breeds PRA has certain common features. Early in the disease, affected dogs are night blind, lacking the ability to adjust their vision to dim light; later their daytime vision also fails. As their vision deteriorates, affected dogs will adapt to their handicap as long as their environment remains constant, and they are not faced with situations requiring excellent vision. At the same time the pupils of their eyes become increasingly dilated, causing a noticeable "shine" to their eyes; and the lens of their eyes may become cloudy, or opaque, resulting in a cataract.

The big difference in PRA among breeds is in the age of onset and the rate of progression of the disease. Early onset forms of PRA occurs when the disease results from abnormal or arrested development of the photoreceptors -- the visual cells in their retina, and affects pups very early in life. Late onset PRA affected dogs appear normal when young, but develop PRA as adults. From what I have learned about the affected Löwchen, the problem is being diagnosed when the dogs are tested prior to a first breeding and all have appeared normal as puppies, but perhaps they were simply 'adapting' to their situation.

Diagnosis of PRA is normally made by ophthalmoscopic examination. This is undertaken using an instrument called an indirect ophthalmoscope, and requires dilatation of the dog's pupil by application of eye drops. Broadly speaking all forms of PRA have the same sequence of ophthalmoscopic changes: increased reflectivity (shininess) of the fundus (the inside of the back of the eye, overlain by the retina); reduction in the diameter and branching pattern of the retina's blood vessels; and shrinking of the optic nerve head (the nerve connecting the retina to the brain). These changes occur in all forms of PRA, but at different times in the different breed-specific forms. Usually by the time the affected dog has these changes there is already significant evidence of loss of vision. This examination is often referred to as the 'CERF' test and must be performed by a board certified ophthalmologist to be eligible for application of a CERF number.

Confirmation of the diagnosis can be undertaken by electroretinography. This is an electrical measurement of retinal function somewhat similar to an electrocardiographic test of heart function, but with two differences: the electroretinogram (ERG) can only be recorded as a response to a flash of light

(i.e.: it is not a free running signal like the EKG); and accurate recording of the ERG requires that the dog be anesthetized. In all dogs showing clinical evidence of PRA, the ERG is severely diminished or extinguished.

The ERG can also be used for early diagnosis of specific forms of PRA, to detect PRA-affected dogs before they demonstrate clinical evidence of disease. This requires very carefully controlled ERG recording conditions, and a well-defined understanding of the age of onset and rate of change of ERG dysfunction in the specific form of PRA under consideration.

With one exception, PRA in all breeds so far studied is an autosomal recessive disorder. This means that to be affected a pup has to receive one copy of the defective gene from both parents. Thus both parents of an affected pup must be either carriers or affected themselves. Also, because affected dogs have two copies of the defective gene, all their progeny will be at least carriers. The genetic chart that I have included in this report illustrates the various combinations of breeding and the results that will be produced.

The recessive gene can hide for generations until two carriers are bred and PRA shows up. A breeder can conscientiously be testing their dog but CERF or ERG testing cannot determine a carrier. The dog is bred and produces a litter and the entire offspring test clear. The dog is then bred to a different bitch and only when a PRA affected puppy is produced will it be realized that the dog is in fact a carrier as is this new breeding partner. This is the true tragedy of PRA - a breeder can unknowingly spread PRA throughout several lines.

Research is underway to develop a DNA blood test can be developed to test for the defective gene. In April of 2003, the Löwchen was accepted into the research project at Ruhr-Universität, Bochum, Germany and pedigrees and blood work have been submitted from five affected Löwchens and 21 of their unaffected sires, dams and siblings. Researcher Tanja Schrameyer promises to email me updates on a regular basis. Recently, Optigen, a research organization in the USA, has expressed interest in our research. Optigen has been instrumental in developing PRA testing for other afflicted breeds. Cornell University has also recently been contacted as they too have developed test for other breeds. Breeders may contact me directly for information if they have information or own Löwchen that would be of interest to the research teams. Any developments will be published here in the newsletter and posted to the LittleLionDog list online.

To help facilitate this research, several of us who have experienced PRA on a personal level (myself, Nadine Baldwin (Java) and Janette Swindler and Jo Beckett (Don Giovanni) have formed a PRA Council. This group is not directly affiliated with either the Löwchen Club of Canada or the Löwchen Club of America. Its sole purpose is to raise funds and collect data to facilitate the development of a blood test. As some of you know, Janette auctioned off two beautiful quilts, Jann has some stunning wooden bowls up for bid, and Nadine & I have donated two classy baskets for raffle at two different shows.

Meanwhile, the best recourse available to breeders is annual CERF exams on all the Löwchen they own or breed, ERG confirmation of any 'questionable exams' and honest disclosure of the problem when diagnosed. This means ensuring 'pet owners' are made aware of the ongoing research and have their Löwchen tested as well to determine if one of them tests positive for PRA. CERF testing is quiet, readily available in most provinces and relatively inexpensive (\$40.00 per exam seems to be the average price for the testing). ERG testing is not readily available and is expensive so if an ERG is indicated, a breeder should consider sharing costs to ensure the test is performed. Since PRA is progressive it is important that repetitive checks are obtained as the dogs age. A single eye check at a young age does not ensure a dog is not afflicted. Remember, the current eye examinations can NOT identify a carrier. It is very important that breeders who produce an affected puppy come forward with this information because it identifies two proven carriers and this information is critically important when researching pedigrees for breeding.

Until the method of detecting the defective gene in carriers is available, breeders must depend upon vigilance, testing and careful research of pedigrees to reduce the occurrence of PRA in the breed.

Cath Horne operates a site called LöwchenWorld (www.löwchenworld.com) and it contains a huge database of löwchen pedigrees from around the world. Breeders are free to access this information to aid them in their breeding programs.

There is also a list of the publicly known cases of PRA. The breeders of these dogs have shared this information with the world because of course; it identifies proven carriers (the sires and dams of the affected dogs). It is very important to understand that for a dog to be a carrier, their sire or dam had to have either been a carrier or affected. (Refer to the genetic chart).

To illustrate the importance of identifying the carriers, I list here the affected dogs and their sires & dams and please note these dogs come from very different breeding lines, which probably indicates the PRA genes are well spread world wide in the Löwchen gene pool.

(Australia) Elguardia Don Giovanni (Elguarda Bailey Boy x Jonquilow Mozarts Melody)

(Canada) Wildhearts Heaven Forbid (Elguarda Appollo Warrior x Wildhearts Against the Wind)

(Denmark) Silver Coats Viva Forever and Silver Coats Sweet Amigo (littermates) (Tiberia Le Petit Phiton x Von Redderkrug Alina)

(Finland) Chic Choix Garcon de Mama (Chic Choix Arc-En-Ceil x Chic Choix Zephyrine Noir)

(Finland) Chic Choix Moiche et Papa (Chic Choix Chic Et Noir x Chic choix Dame De Coeur)

(Finland) Lionlife Liberty Street (Chic Choix Deric Beauvoir x Chic Choix Oiseau De Venus)

(Germany) Trusty Friends Alec & Trusty Friends Beauty (repeat breeding) (Von Kieselgrund Percy x Vom Stolzenwald Angie)

Until a genetic blood test is available that will determine almost at birth which löwchens are affected, which are carriers, and which are clear, it is up to breeders to do pedigree research prior to planning a breeding. Breeding is not advised for any dog with PRA, or for the parents (carriers). Keep in mind the parents of the parents have produced a carrier and try to avoid doubling up on these particular dogs for 3 or 4 generations. Also note the earliest diagnosed PRA affected löwchen to date has been age two so it is advised that repeat breedings not be done until all puppies from the first litter have CERF tested clear at this age. These are only precautions and will not guarantee more PRA affected löwchens will not be born. At this point in time there are obviously many unknown carriers in the gene pool and it is highly possible that two carriers will be inadvertently bred.

This is why sharing of test results is so very important. It is important to remember this is not a condition isolated to breeders whose breeding programs are based on line breeding - my PRA affected Java was a result of a complete outcross for 5 generations nor is it a problem that exists in one kennel or one line. PRA is not an isolated problem in our breed so let us not isolate those breeder who have the integrity to 'go public' with a PRA positive test result Every breeder must commit to testing and yes, contributing to the research for this is a serious problem that effects OUR BREED!

jayne osburn-lapointe

wildheart löwchen

bc canada

"try to be the person your dogs think you are"