PRA Update in the Toller

This is an update to articles that have been published previously in the Spring and Winter 2002 issues of Quackers. It was written by Jane Folkman in consultation with Dr. Sheryl Krohne, DVM, MS, Diplomate ACVO and Genetics Committee CERF Liaison, Dr. Gus Aguirre, Jeanette Felix, President of Optigen and Sue Van Sloun. Special thanks those who contributed information about living with a PRA affected dog.

Since the Optigen PRA test was introduced in February, 2002 there have been 990 Tollers tested worldwide, with about 49% Pattern A, 44% Pattern B and 7% Pattern C. These statistics are as of June 30, 2004. ***Optigen and experts recommend that one Pattern A dog be used in each breeding to reduce the incidence of PRA.*** The purpose of Optigen, Canine Eye Registration Foundation (CERF) and the American College of Veterinary Ophthalmologists (ACVO) Genetics Committee recommendations is to help breeders avoid perpetuating eye diseases like PRA.

There are currently eight disorders for which CERF and the ACVO Genetics Committee has the unequivocal recommendation against breeding in all breeds, including the Toller. These conditions frequently result in blindness. Two of the eight disorders include **catatacts** unless the eye vet has noted "significance of above punctate unknown" and **Progressive Retinal Atrophy or PRA.**

Breeders and Toller owners may mention that PRA is a late onset disease in Tollers and does not affect their vision until later in life. A recent statistical study commissioned from CERF by us actually shows that about 52% of the Tollers diagnosed suspicious for PRA were diagnosed by age 4 with the earliest detection between 1-2 years. The remainder (48%) were diagnosed after age 4. Please refer to Table 2.

Table 2. PRA in Tollers, 1991-2003 CERF Data

The categories of Retinal Atrophy – generalized and Retinal Atrophy – suspicious have been added for each year.

	No. of Dogs
+ indicates Tollers diagnosed with Retinal Atrophy – suspicious	47
* indicates Tollers diagnosed with Retinal Atrophy – generalized	19

Age of Diagnosis	Number	Percentage	Graph	
0-1 year	1	1.5%	+	
1-2 years	9	13.6%	+++++++++	
2-3 years	12	18.2%	++++++++++++	52%
3-4 years	12	18.2%	++++++++++**	

4-5 years	7	10.6%	++++++*	
5-6 years	15	22.7%	+++++**********	
6-7 years	3	4.6%	++*	
7-8 years	2	3%	++	48%
8-9 years	0	0%		
9-10 years	3	4.6%	***	
10+ years	2	3%	**	

For this PRA CERF study, we picked the first visit when the disorder was diagnosed for each "PRA" dog to detect the age of onset. The Chair of the ACVO, Dr. Sheryl Krohne advised adding the PRA categories as the best approach to get all the dogs with "PRA" because vet ophthalmologists often note PRA – suspicious, then recommend another exam in a year. Future exams would most certainly determine the PRA diagnosis, but unfortunately and in reality, breeders may not keep the dog or follow their eyes if a CERF certificate cannot be issued.

This new CERF study reconfirms that eye vets can see signs of PRA in the Toller at various ages. Research has shown that unlike other breeds, Tollers have a broader timeframe when PRA develops - some early and some late - and can exhibit a variable rate of disease progression.

If a breeder mates two Pattern B dogs, genetics demonstrate that 25% of the dogs will be pattern C or PRA affected. If one is under the assumption that PRA may not affect the dog until later in life, this may or may not be so. Thirteen years of CERF testing shows that 52% of Tollers had suspicious symptoms of PRA that could be seen by indirect ophthalmoscopy examinations at age 2, 3 and 4.

The *prcd* or progressive rod-cone degeneration form of PRA in Tollers is a "late-onset" disease. That is, the disease develops after the normal differentiation of the retinal visual cells. Most dogs with "late-onset" PRA develop clinical signs between 4-6 years of age. In some Tollers, opthalmoscopically evident disease is present in older dogs, around 6-8 or even later. The gene causing the "standard" (ie. 4-6 years) and "late onset" (ie. 6-8 years) prcd form of PRA is the same. It appears that modifier factors-meaning other genes-modify the age of onset. This is still a research mystery that Dr. Aguirre and his team is trying to unravel.

With Dr. Aguirre's research, Tollers have been diagnosed with PRA over a very wide age range – as young as 3 years and as old as 9 years. However, based on the new CERF study, it's clear that some Tollers are suspicious for PRA even earlier. And although no one can predict which dog will have more or less vision impairment, it is important to be aware of the relative risks and results of mating two Pattern B dogs which can result in producing PRA affected puppies.

Also often seen with the progression of PRA is the eventual development of bilateral cataracts in many affected dogs. Several studies in other dog breeds, such as the Labrador Retriever, have established an association between PRA and the early development of cataracts that precedes the old age cataract formation in all breeds. Some PRA Toller owners have seen cataracts develop as early as age 7. Cataracts and visual degenerations interfered with field training in the case of Abby. Abby's owners, the Milburys, noticed she began having difficulty seeing marks, especially on cloudy days. Abby's PRA and bilateral cataracts ended her field career sooner than her owners would have liked. Within one year of her initial diagnosis with moderately advanced PRA at 8, Abby already had bilateral cataracts. A year later the cataract development was so severe the ophthalmologist could not determine the progression of her PRA. Abby, now 15, has been essentially blind since age 9 and has been confined to the yard or house. The cataracts that develop with PRA affected dogs can be considered an accelerated form of old age cataracts, according to Dr. Gus Aguirre. ACVO experts say that old age cataracts do not usually develop until the age 11 or 12.

This is why experts recommend that one pattern A dog be used in each breeding, so that disease like PRA and the secondary cataracts, will not be produced.

In general, it usually is the prcd form of PRA (as it is major inherited retinal disease in breed), but can also represent another retinal degeneration, which can be inherited, but not be prcd, or represent an acquired disease that is not inherited. Since OptiGen provides free DNA testing for any dog that has a diagnosis of PRA (as long as it is accompanied by a pedigree and a copy of eye exam by an ACVO diplomate), it is essential that all dogs that have a diagnosis of PRA have also a free DNA test. For more information, please refer to the Optigen website: www.optigen,com or contact them by email at: genetest@optigen.com.

Living with a PRA Affected Dog

To better understand the effects of PRA, several folks who have had or still live with PRA affected dogs were intereviewed. As mentioned above, Tollers have a broader timeframe when the disease develops - some early and some late - and can exhibit a variable rate of disease progression. This proved true to form.

For example, Jenny, a key individual in the PRA research effort, did not show vision loss from PRA nor did a CERF detect it when she was 8. This holds true for Rusty who also tested PRA C, yet at age 7 his CERF exam remains clear. Both dogs probably have an incomplete penetrance of the disease and thus exhibit no noticeable vision changes.

However Rusty's littermate Rover began to show signs of diminished vision on long marks in field training, especially on cloudy days, when he was 5 years old. He is also Pattern C and his eye exam showed suspicious PRA at age 4. This reconfirms there are wide variations in the age of onset and effects of PRA, even within a single litter.

Smitty was diagnosed with PRA at the age of 3 1/2 and developed cataracts around the age of 9. His noticeable changes were in his side vision and transitioning from bright sun to shade. Eventually Smitty developed hearing loss and the combination of lack of hearing and no vision was the deciding factor in putting him down. If he had one or the other, he would still be with us according to his owners, but the two conditions together did not give him the quality of life that is needed for a Toller. His PRA was heartbreaking for his owners, however Smitty was irreplaceable and contributed much to the PRA study and educating people about the day-to-day effects of PRA.

In Rem's case, his owners first noticed he could not track a tennis ball in dim light when he was about 2 year old. Just before age 4 his CERF exam was suspicious, but further vision loss was not noted until 7. By age 8, cataracts were beginning to form. But Rem adjusted and was still able to compete in agility, obedience and flyball until 10. At age 12, Rem's owners think he can only see blurry, large-scale motion, but says he has lived a happy life. He interacts with their other Tollers and people and sits outside and watches (in his own fashion) the world go by. You see, Rem does not know life any differently.

These articles are based on the science available and expert opinion, however, to those who have had or have PRA affected dogs and worked hard to help develop the Optigen PRA test, it is important that Toller owners and breeders be educated about the disease. Living with a PRA affected dog may or may not be a significant challenge. It depends on the severity of the vision loss, cataract development and needs of each particular dog and family. But how is one to know all this when the Pattern C puppy is born?