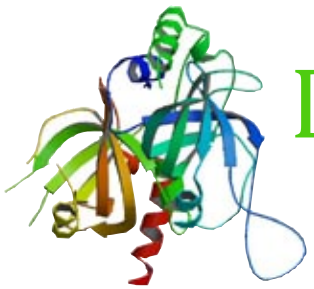


Defect Genes & Inbreeding

When an outcross breeding isn't an outcross breeding

By Sy Guth

Recently I was tracking a defect in a breed back to its likely origins. In the process some interesting things about inbreeding versus outcross breeding became evident. This article is a summary that takes data from the original 20-page paper, but gives the breed and the trait another name and summaries the important bits. The inbreeding scenario is likely to be the same for many breeds with a young history (less than 200 years). Because we live in a small country (in terms of number of dogs) our dog gene pool is always challenged. But in the case of this breed and defect, even the mother country of the breed with its great number of dogs is subject to the defect and at the same percentage of occurrence as seen in Australasia.

The Quest to Find the Original Defect Carriers

We will call the breed the Happy Doggy Breed. It is one of the top 10 dog breeds worldwide. The breed was founded about 150 years ago and was developed from three other breeds of dogs for a specific purpose.

The defective trait we will call the Rainbow Bridge defect because the trait, when manifested, usually ends with the affected puppies being given sleep before they are 1-year-old. It is normally detected prior to 3 weeks of age and the puppies are given sleep at that time. The defect we are tracking back in time in our breed occurs about 1% to 2% of the time in the breed and is a polygenetic gene (having more than 2 genes involved – it is assumed there are 5 or 6 genes involved) and assumed to be a recessive gene (needing both parents as carriers to produce it).

I was given a good number of litter pedigrees that had produced the Rainbow Bridge defect. We (royal "we") start looking at the pedigrees of litters that have produced the defect and quickly spot a starting point with a dog that appears on both sides of a pedigree. This dog is of interest because it had stood out (along with four other dogs) in a number of pedigrees in a European country relating to another defect. We then find this dog in other affected pedigrees and follow the trail back in time. Then referring to papers other breeders and a vet have written on the defect some 30 years ago, we note that these breeders had also picked up on the same ancestors. These early researchers tracked the defect back to the 1950s without the help of today's computers.

We use a couple of sophisticated breeding software programs – one with complete pedigree data back to 1900 for dogs in the originating country of the breed and the other with significant data back to 1900 that includes dogs from Australasia and the originating country. After 10-days of intense tracking, we find a pair of dogs from the 1930s we think are strong carriers of the defect. The defective genes may go back further, but things start to get a bit cloudy in the pedigrees at this point, so we stop with this pair of dogs. We'll call the pair of dogs in the 1930s Sparky and Lady.

As we move forward again in time, we note that these early dogs appear in certain pedigrees multiply times and with a good deal of inbreeding in the first 5 generations. We also note that three kennels seem to be using the dogs the most and note the number of children and grandchildren from our "suspect" early dominate dogs.

We make a list of more "suspect" dogs by following the off-spring lines of the dogs where two suspect carriers were mated. *Fig 1*

The number of off-spring for these dominate carriers brings a feeling of despair as we realise these early suspect carriers are behind every dog in our breed worldwide. This is due to the fact that nearly all the suspect carriers were champions and popular breeding dogs.

Dog	Children	Grandchildren
Tuff (1929) sire of Sparky	150	909
Sparky (1931) sire of Sam	229	850
Sam (1938) sire of Scamp	154	1,332
Scamp (1945) sire of Kim	42	328
Kim (1948) sire of Jason & Laddie	174	961
Jason (1949)	148	790
Laddie (1951)	300	2,029

Fig 1

As we progress in the study, we see trends in dogs and kennels and create four groups:

- Group 1: The original pair of dogs – Sparky and Lady
- Group 2: 8 dogs that seem to be particularly significant due to inbreeding with the original pair of dogs.
- Group 3: 12 dogs whose kennel used the dogs from group 2 and intensely inbred. This included full-sister to full-brother and father-to-daughter breeding.
- Group 4: 5 dogs that are litter mates. This is the group of dogs the early researchers targeted as well as one of the dogs in group 2.

Our four groups of dogs used for calculating profiling statistics are heavily inbred dogs directly related to the suspected significant carriers – the original pair of dogs.

Creating a Profile for Past Carriers and Current Affected Dogs

The software we are using has some advanced features in terms of inbreeding of COI (Wright's Coefficient of Inbreeding). The normal stats provided in most breeding software is a list of all the ancestors behind the dog shown once and gives the COI percentage, COR percentage, and line-breeding position for each of the ancestors. COR is the Coefficient of Relationship and estimates the probable percentage of blood genes passed down from an ancestor one time only. This is all normal standard information you would expect to see from a computerised breeding database.

However, our advanced version of the software provides two other important statistics for our profiling. One is a count on the number of times an ancestor appears in the pedigree. The other feature is the Blood-Percentage. This Blood-Percentage figure is different from the COR and is the percent of blood-genes based on **all instances that the ancestor appears in the pedigree**. In other words, it estimates the chance that the genes from said ancestor might be contributed by a parent in a mating.

Parents who threw Rainbow Bridge Puppy after year 2000 ↓	(Suspected significant carriers of RB Trait →)	Group 1 (2 dogs 1930s)	Group 2 (8 dogs 1947 - 1962)	Group 3 (13 dogs 1953 - 1964)	Group 4 (5 litter mates 1957)	Group Totals	Total Blood-gene % of all ancestors in pedigree	Extracted % of Blood-genes for Group Total
SIRE - WPL06SX3	Count of # of times ancestors appear in pedigree for each group	53,064	6,280	774	71	60,189		
	Blood-Gene %	33.23%	94.97%	18.32%	2.00%	148.52%	2234.00%	6.65%
DAM - WPL4-6DX2	Count of # of times ancestors appear in pedigree for each group	53,836	5,762	716	149	60,463		
	Blood-Gene %	33.30%	85.04%	21.21%	8.31%	147.86%	2243.00%	6.59%

Fig 2. Sample profiling for a set of parents who manifested the Rainbow Bridge defect in a litter.

Using the four groups of dogs, we profile dogs that have produced the Rainbow Bridge trait by noting the number of times the ancestors for each of the four groups of dogs appear in the affected dog's pedigree. We then note the Blood-Gene percentage for each of these four groups. We see a trend forming and note that the original pair of ancestors – Sparky and Lady are each contributing 10% to 40% blood-genes to the affected dogs. The four groups of dogs are contributing over 100% of blood-genes. We also note that each parent, in *Fig 2*, had more than 53,000 instances of the two original pair of dogs. These parents produced the defect in a litter of puppies after year 2000. We are surprised that dogs all the way back to the 1930s to 1964 are contributing such high percentage of blood-genes in today's dogs. *Fig 2*

We then total the four groups of Blood-Gene percentage. When we sum the total Blood-Gene percentage for all the ancestors in the pedigree and divide it into the total percentage for the four target groups of dogs. This determines that the current affected dogs are showing around 6% to 7% percent chance of inheriting genes from the historical affected dogs in our four groups of suspected dominate carriers. This means the puppies stand a chance of inheriting 6% to 7% defective genes from each parent. After profiling over 30 affected dogs, we profile some non-affected dogs and note that these dogs often do not have any instances in groups 3 and 4. We decide our crude profile analysis is showing trends sufficient to get a feel for the "dominate" carriers.

Pedigree Charting and Evaluating a Pedigree

To help further understand the depth of this Rainbow Bridge defect problem, we decide to do some pedigree charting and that is when we discover some things about breeding that we had not noted previously in regards to the concept of inbreeding and outcross breeding. We know our "dogs of interest" are champions and have been used heavily for breeding and realise that finding the DNA markers will be the only way to ascertain if a pair of dogs is likely to throw an affected puppy in a litter. We also realise we will never be able to rid the breed of the defect.

It is common for most breeders today to look at a 5g pedigree as one of the means of determining a successful mating. They compare the dam's pedigree to that of the sire. If one does not see any common ancestors in the first 5g, one tends to refer to the mating as an "outcross" – no common ancestors between sire and dam.

It has been said by some "old-time" breeders that if there are 42 to 48 unique ancestors in a 62 ancestor pedigree (5g) that this is a good line-breeding. This has been learned from the long-time breeders. However, what held true 50 years ago, may no longer hold true for the breed today. This is illustrated in the pedigree charts that follow. The charts go back to approximately 1900, as that is the point in time when the breed linage can most accurately be traced. Prior to 1900 there were gaps and questions as to ancestry. So the following pedigree charts will show up to 100-years plus of repeat ancestors.

We are going to use two couples for the pedigree charting. The names in the first 5 generations of each pedigree have been substituted with codes.

The first set-of-parents are from the "home country", were mated in 1969, and have repeat ancestors in their 5g pedigree. The number of repeat ancestors is reflected in the ped chart. The ped chart for this 1969 couple goes back 33 generations. The second set-of-parents are from NZ and were mated in 2007, and charts back to the same point in time as the first set-of-parents – approximately 1900. This 2nd set of dogs has 57 generations in the pedigree chart. The 2007 set of dogs was chosen because it was a total outcross mating between the sire and dam based on the first 5 generations – eg no common ancestors in the first 5g between sire and dam. We also chose it because it produced a Rainbow Bridge puppy in the litter – showing that "outcross breeding" does not reduce the chance of producing a breed defect. On the sire's side there is one common ancestor at the 4g and 5g level and one more common ancestor at the 5g level. On the dam side there is one dog repeated at the 4g level. Both 5g pedigrees are relatively free of repeat ancestors and this is evident in the elongation of the 5g and 10g pedigree charts compared to the 1969 charts. *(Figs 4 & 5)*

From the number of generations in the two sets of pedigrees, we can deduce that the breed, from 1900 to 1969 was producing just under 1 generation every 2 years and from 1900 to 2007 it has produced just over 1 generation every 2 years. The current day issue is the number of generations going back to 1900 has increased significantly, but the percentage of unique ancestors has not**. In fact, the number of unique ancestors in a mating today is a fraction of what it was less than 40 years ago**. This is why the percentage of blood-genes from the early carriers remains so high. The following is a chart showing the percentage of the unique ancestors for the two couples. *Fig 3*

Name	Total Ancestors	Total Unique Ancestors	Percent of Unique Ancestors
"P1" couple (1969) 33g	1,835,815	784	0.042706
"G1" couple (2007) 57g	1,776,196,157	3,155	0.000178

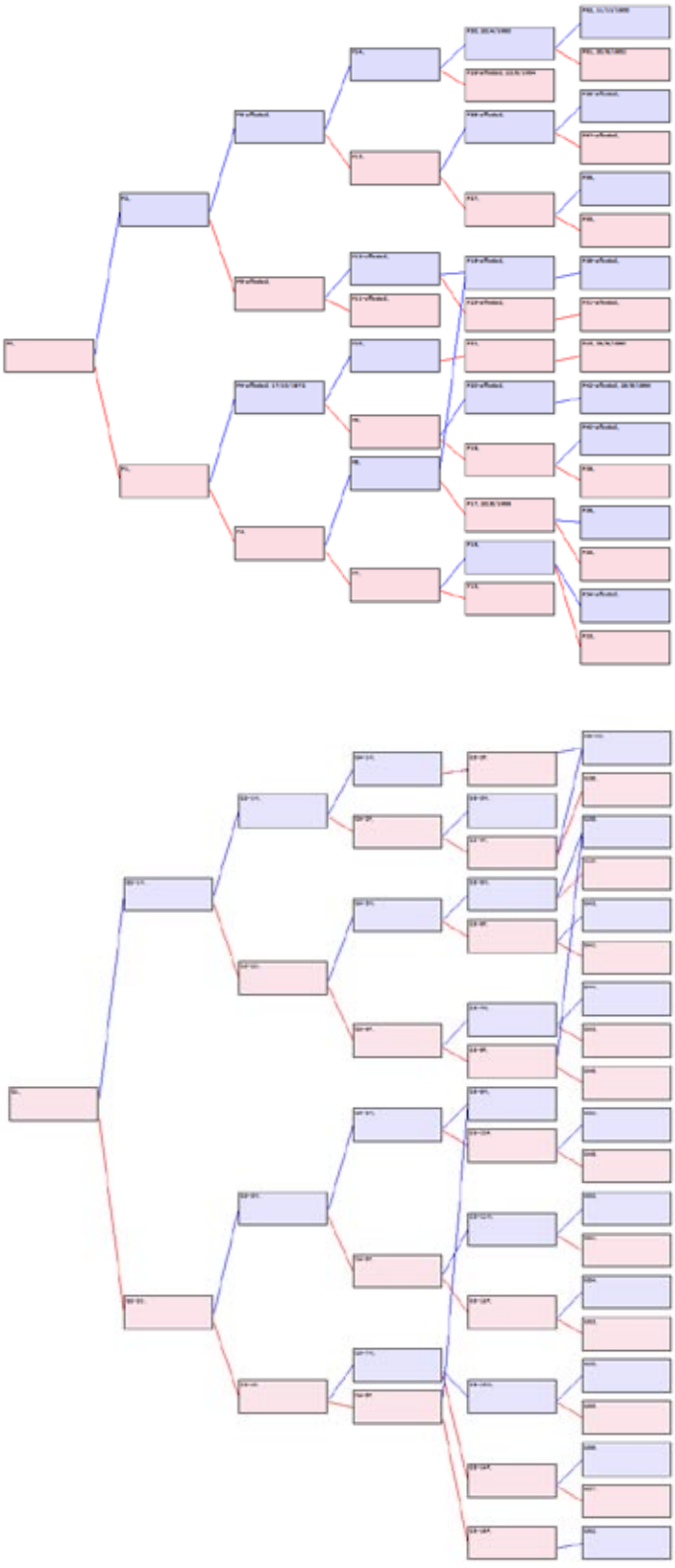
Fig 3. Data from an authenticated database with complete ancestor lineage back to 1900.

This information reveals that comparing a 5g pedigree is a shallow and self-deceptive way to understand the Russian roulette of the gene pool scenario. If one goes back just a few more generations from 5g, one begins to see the common ancestors. And if one goes back all the way to 1900 in a pedigree, one gets a very different feel for the breed.

These pedigree chart illustrations are significant because of the blood-gene percentages from the early dominant carriers that still show up in today's dogs.

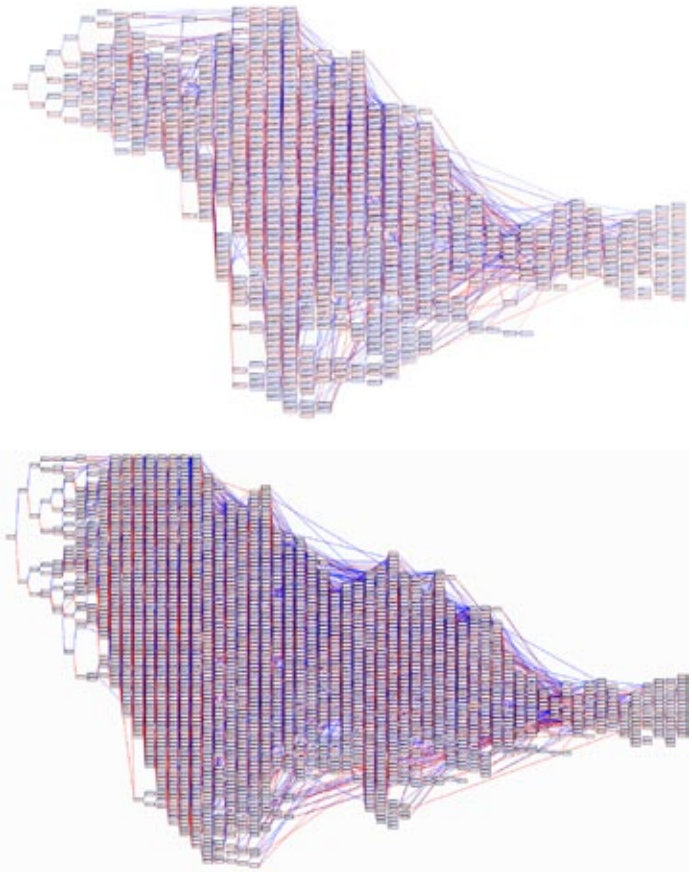
The following illustrations are not intended to be legible. What is of interest is the number of unique ancestors and the "lines" on the charts. The red lines are the dam lines and the blue lines are the sire lines. The charts include 5g *(Fig 4 & 5)*, 10g *(Fig 6 & 7)*, and the "full generation" *(Fig 8 & 9)* back to 1900 for each of our two sets of parents.

Note: the pedigree charting ONLY shows DUPLICATE ANCESTORS. It does not include all ancestors.



Figs 4 & 5. 5g ped charts for the 1969 couple and the 2007 couple

Figs 6 & 7. 10g ped charts for the 1969 couple and the 2007 couple



Figs 8 & 9. 33g ped chart for the 1969 couple and 57g ped chart for the 2007 couple

If we look at the two full ped charts *(Figs 8 & 9)* we can see the same configurations in both – the 33g ped chart is reflected in the right side half of the 57g ped chart. But the density of the inbreeding in the 57g ped chart is far greater than the 33g ped chart.

And this, very simply, is why without DNA profiling and testing we will never be able to sort out the defective carrier genes for any dog in today's breeding programme.

Summary Points for the Study

From the study and today's breeding practices, we can draw some significant points:

- Looking at a 5g pedigree alone to help determine a mating may not provide the information needed concerning inbreeding.
- Doing an "outcross" mating based on the 5g pedigree produced the Rainbow Bridge trait even though there were no common ancestors in the first 5g between the parents. Therefore, an "outcross" mating may or may not have any bearing on defective traits.
- Breeders that have a defect appear in a litter should not feel they need to hide it since, more than likely, they inherited the problem – they did not create it.
- Not talking about defects (the hush-hush syndrome) only leaves other breeders open to having the problem show up unexpectedly and does nothing to help eliminate the defect from the breed or help veterinarians understand if the congenital defect is hereditary and how common it might be.
- The "home country", with its rich resource of dogs and great gene pool, still produces the Rainbow Bridge defect today. NZ is at greater risk because of the small gene pool in our breeds. Yet the percentage of defects occur on a similar scale.
- The only way a defect gene can be ascertained today is through DNA testing of both parents because of the low percentage of unique ancestors in a 100-year pedigree.

DNA Studies

If a defect is of a concerning nature, breeders should seek out institutions willing to take on a DNA study to find the markers for the defect. Often these studies start out with the breeders and researchers funding the early part of the study themselves.

Except for general DNA profiling of the canine, specific defect DNA testing is normally breed specific. In the case of the Rainbow Bridge defect it is not unique to just one breed. So hopefully, when the DNA markers are found for the first breed, it will prove easier for the scientific researchers to find the markers for the other affected breeds.

This study pointed out how shallow the reporting perspective from BBC and the local TVNZ program was in regards to inbreeding. They suggested that cross-breeds have less defects. One can see from the foregoing that this is total rubbish. The breed we looked at was a cross-breed 150 years ago. The same thing will happen to other cross-breeds. To say that cross-breeds are healthier is a mis-guided assumption. The chance of recessive genes meeting in cross-bred parents in the first few generations may be low, but once the off-spring become carriers through one parent, then the stage is set for reproducing a defect down the road. Cross-breeding will just spread more defect traits to a larger population of dogs.

Furthermore, today's cross-breeds do not have health checks applied to the parents before mating and will never be able to be DNA tested for defects because the DNA tests are breed specific. Locating the markers for defects in a specific breed of dog is a long journey and requires time and funding that is hard to source today. The DNA study for the Rainbow Bridge defect was picked up by Massey University, but has not progressed due to lack of funding. At the time of completion of the recent paper I wrote on the defect I was researching, we had a commitment from UK Animal Health Trust to accept and store samples from affected and non-affected dogs until the funding could be found to test the DNA for the gene markers. They needed a minimum of 48 samples to start a study. Another breeder in the UK who has been interested in the defect for many years is now progressing the funding issues. We hear a lot about DNA testing today, but it is not as advanced or as easy in the canine species as we may think.

As breeders, we do need to be responsible and not breed closely related relatives. Until we have DNA tests for specific defects, responsible line-breeding is not going to make much difference in regards to defective traits that materialise 1% to 2% of the time based on the historical information in our sample breed. We should refuse to accept tar and feathering from a reporting press that do not understand the depth of genetics within canine breeds. It is easy to cast out generalised statements. But these generalised statements are nothing more than absurdities when a problem has existed for nearly a 100 years and dominate carriers of the trait appear in every dog in the breed worldwide. Bear in mind, the information for the paper was based on one of today's 10 most popular breeds worldwide.

Every breed has some sort of defect – just as every human being has some sort of defect. There is no such thing as a perfect dog or a perfect person. Nature is what it is. And let's face it, most of us enjoy the diversity of human and animal nature. So we have to accept there are defects as part of that diversity. It's a crazy world we live in when one thinks about it – we don't apply health screen testing to humans in regards to breeding to determine what the off-spring results might be. Humans breed because of romantically falling in love, or sexual drive, or because of family customs. And before someone suggests that maybe we should let our dogs romantically choose their partners. The first litter with a Rainbow Bridge defective puppy for me was one of my girls showing no interest in the dog being considered as her partner and taking herself off across the yard to a near paddock and parading herself in front of one of the breeder's other dogs. Since both dogs were very acceptable she was allowed to breed to the one she had "eyes" for. So romantically based breeding is not the answer either.■