# Genotype Probabilities

# for Canine Lens Luxation in the German Jagdterrier Breed

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Lens Luxation (LL) in dogs is well known as a serious defect of the eye, mostly reported in Terrier breeds. The lens is normally held in position by small fibers, the zonules. If these zonules get week the rupture can cause Lens Luxation. A genetic predisposition was obviously but the mode of inheritance was not quite sure for long time. Some authors postulated a single gene, autosomal recessive inherited, but the age of onset, mainly between 3 and 6 years of age, sometimes later, made it difficult to compare the occurrence of real cases of LL with the expectations from the mendelian theory.

Under the impression that some sire's progeny have high rates of LL with early affection and some others have a very low percentage with late age of onset, the breeding program of the German Jagdterrier Club started breeding value estimation for LL-liability in the early 80th under the polygenetic model. The breeding values are routinely available for all breeders. A PC-program DOGBASE, updated all 3 months, allows complex searching for fitting mates in respect to LL and others traits concerning hunting ability.

Breeding values are published as relative values with a population average of 100 and a standard deviation of 10 points. Affected animals, because of the asymmetric distribution, have breeding values around 170. Best animals reach values between 80 and 85. The breeding plan of the club, mandatory since 1992 for all breeders, allows only matings in that way that the average breeding value of both parents has to be better (lower) than 105.

In her theses Scheler (1995) compared different models of inheritance. She found a recessive major gene, with a minor additive genetic modification variance, as the most probable mode of inheritance. The calculation of Genotype Probabilities for that major gene was compared to the Breeding Value Estimation. The power of prediction was tested for both techniques and they did not differ. So there was no need to change the whole breeding policy, the orders and the established routine.

The frequency of LL in the breed could be reduced. The low number of cases makes breeding value estimation, from a numerical point of view, more and more difficult. While under the recessive genetic model one affected child identifies the parents to be heterozygous and all the preceding unaffected siblings are ignored, the breeding value estimation keeps all that information about the unaffected children. This gives relatively good breeding values if the affected animal comes after a long serie of unaffected children and it gives high values, bad values, if the affected animal occurs early.

Because of those problems the genotype probabilities are calculated additionally to the breeding values to give the breeders and the consultants the chance to compare. Breeders will be trained the next time to use the new type of information.

**Estimated Genotype Probabilities (EGP's)**

***Genefrequency:***

Most defects are caused by a single mutation in a autosomal gene. The symbol for the mutated allel may be **a** and for the normal gene may be **A**. In each individual dog always two allels exist, one comes from the father, one from the mother. Three possibilities exist for the two allel combinations:

*AA*, *Aa* and *aa*.

The frequency of the mutated allel in the population is named „gene frequency of **a**" which corresponds with the gene frequency of **A**. Both sum up to 1.0 or 100%.

If the genefrequency for **a** may be q=0.10 or 10%, and for **A** by that is p=0,90 or 90%, then the three genotypes occur with the following combination probabilities:

AA ➔ 0.90 * 0.90 = 0.81 ➔ 81 %

Aa ➔ 0.90 * 0.10 = 0.09

0.18➔ 18 %

aA ➔ 0.10 * 0.90 = 0.09

AA ➔ 0.10 * 0.10 = 0.01 ➔ 1 %

If in a population under random mating 1% affected animals occur, then the genefrequency for the recessive gene in the population is 10% (the square-root from the rate of affected animals). For Lens Luxation (LL) the gene frequency in the Jagdterrier population on an average of the last 55 years must be assumed to be 0.21.

***Genotype probabilities of an individual:***

The calculation of genotype probabilities is a complex mathematical procedure. It outputs three figures, the probabilities to be of type ***AA***, ***aA*** or ***aa***.

The first steps in calculation seem to be simple. All affected animals are of type *aa,* so the Genotype probabilities are

0, 0, 1

which means that they are not of type *AA*, not of type *Aa* and 100% sure of type *aa*. Parents of affected animals, itself not affected, are of type *Aa*, so the 3 probabilities are

0, 1, 0

which means that they are identified with 100% probability as heterozygous. They must be of that type because they both transmitted one Gene **a** to the affected child. They can therefore not be of type *AA*, on the other side they are not affected which excludes the type *aa.*

In Lens Luxation the problem exists, that some dogs of type *aa* are not observed to be affected. This is named *incomplete penetrance.* May be they died before the age of affectedness, but they have offspring. Then there is a low residual probability to be of type **aa**, for example

0, 0.95, 0.05

The examples given before are quite clear, but sometimes the genotype is not sure. If one dog in a litter is affected and three others are well, then both parents are heterozygous, as mentioned before. But of what type are the unaffected siblings? From the mendelian rules we know, that 25% are of type *AA*, 50% are of type *Aa* and 25% are of type *aa*. The last type we can identify by LL. The remaining healthy dogs can be of type *AA* (one third of the healthy) and of type *Aa* (two third of the healthy). So the probabilities are

0.33, 0.67, 0

for all of them. There is at this moment no chance to differ of what type they really are. Only if they are used for breeding the results from the progeny make the probability higher for AA, if no cases of LL are reported and make the probability for Aa higher, if affected descendants occur. *Aa*-probability jumps to one, if a direct child is affected and grows, if affected animals occur in the second or third generation.

However, for all animals of the whole population finally a list of genotype probabilities exists, which can be submitted to the breeder to help him in his decisions. But what is the real risk of matings?

***Probability of Transmission:***

The transmission of a mutated gene from a dog or from a bitch to the progeny depends on the genotype. If the animal is affected and has the genotype *aa*, then 100% of the gamets (sperms, ova) will carry the mutated gene. The probability of transmission P=1.0.

If the dog is of type *Aa*, every second sperm will carry the gene **a**, the transmission probability P=50%. In the case of genotype *AA* the probability P=0. If there are different genotypes possible for one individuum, the P-value can be calculated by taking half of the genotype probability of *Aa* plus the full genotype probability for aa.

Some examples:

Genotype probabilities: 0.00, 1.00, 0.00 P = 0.50

0.33, 0.67, 0.00 P = 0.33

0.25, 0.50, 0.25 P = 0.50

1.00, 0.00, 0.00 P = 0.00

***Genetic Risk:***

The disease can only occur, if the mutated gene is transmitted from father and mother at the same time. This combination probability **a** from father combined with **a** from mother is the product of the transmission probabilities of both parents. For example, if the father is heterozygous with P = 0.5 and the mother is also heterozygous with P = 0.5, the risk for a child from this mating is 0.5 * 0.5 = 0.25 or 25% to be of type *aa*, which is in agreement with the mendelian rules. If a bitch of type *Aa*, P = 0.5, is mated to a male of type *AA*, P = 0, the risk for the puppies is 0.5 * 0 = 0. No puppy will be on risk, half of them will be heterozygous, but they will not be affected.

***Consequences and breeding strategies:***

If the breeding goal is, to breed healthy, not affected dogs, the breeding strategies must be to breed puppies from parents in that way, that the P-value of the father times the P-value for the mother is zero. Well, zero may be to extreme because there is no chance to breed in a population with a gene frequency of 10-20% with **no** risk. If at this moment the rate of affected dogs is 1%, the risk can be reduced to 0.5%. Then the next step is done. It can be suggested to breed puppies with a maximum risk of 0.5%. It is the free decision of the breeder, to breed on a lower risk level.

***Conclusions:***

The German Jagdterrier Club actually has a breeding plan, which is based on breeding values. It has to be changed to the genotype probability technique. First experiences show that the clear rules of mendelian inheritance are well understood and accepted by the breeders. The progress in combating the disease must be observed to verify, that the major gene for LL is the only important reason for LL and the modifying genes are without effect, if the main mutation does not exist.