Using Relative Risk Pedigree Analysis and Open Health Registries to Plan Matings

By Jerold S Bell, DVM, Tufts Cummings School of Veterinary Medicine

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Breeders strive to balance selection for the positive aspects of their dogs with selection against genetic disorders. Unfortunately, at this time most hereditary disorders do not have genetic tests for carriers. With polygenic disorders, or those with an unknown mode of inheritance, breadth of normalcy in the pedigree is the best selection tool. (See "Breeding Strategies for the Management of Genetic Disorders" in the "Healthy Dog" section of the November 2001 *AKC GAZETTE*.) Without tests for carriers, the most objective tool for selection against recessive disorders is relative risk pedigree analysis based on the knowledge of proven carrier and affected dogs in the pedigree.

Successful use of relative risk pedigree analysis requires a proven recessive mode of inheritance, confirmed diagnoses for the condition, and verified pedigrees. The best way to work with this information is through a breed club supported open health registry. Many national breed clubs maintain health registries through the Orthopedic Foundation for Animals (OFA), the Institute for Genetic Disease Control (GDC; which has now merged with the OFA), the Canine Health Information Center (CHIC), or though their own club or health foundation.

For relative risk analysis to be useful, the knowledge of all affected and carrier dogs is necessary. This requires an open health registry, relying on an atmosphere of cooperation and understanding between breeders, for the benefit of the breed. Breeding practices do not cause defective genes. No one wants to produce affected dogs, or propagate a genetic disorder. If breeders are reluctant to identify affected dogs, then the usefulness of relative risk analysis will be limited.

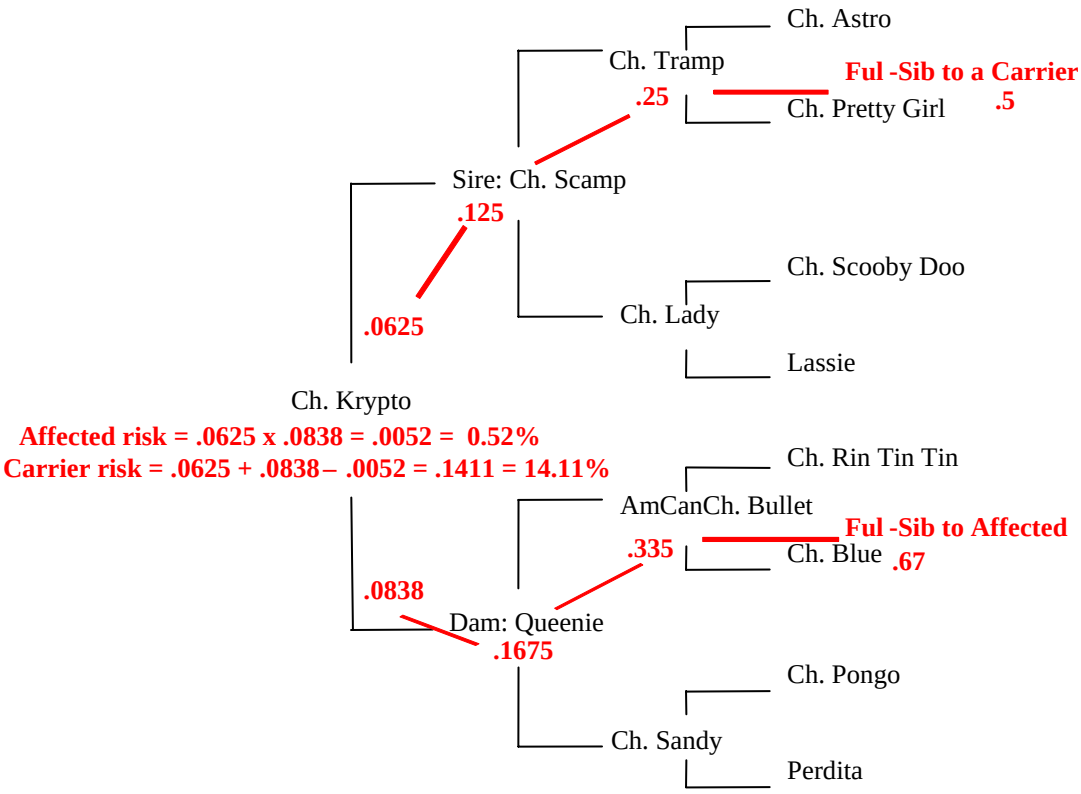
With a simple autosomal recessive genetic disorder, pedigree analysis can be used to compute relative risk factors for carrier and affected status. The following are the objective risk factors for a simple autosomal recessive gene: Parent of affected (and therefore a carrier) = 100% (chance of being a carrier); offspring of affected = 100%; non-affected full-sibling to affected = 67%; full-sibling to carrier = 50%. Similar risk factors can be calculated for x-linked recessive disorders.

Sometimes breeders want to add risk factors for each parent of proven carriers. Only one parent of a carrier needs to pass on the defective gene, but it often cannot be determined which one is a carrier. Assigning carrier risk to both parents falsely places selective pressure against dogs based on their matings, and not their proven genetic background. Therefore, risk can only be assigned when the parents of confirmed carriers are mated together.

Determining relative risk in a pedigree involves identifying every individual with objective risk from the above categories and calculating the risk from the oldest ancestors in the pedigree down to the individual whose risk you want to identify. To calculate the risk, use the number designation (.50) versus the percentage (50%). From one generation to the next, if the risk is coming from only one side (either the sire or dam), then the offspring's risk is one-half of the risk from the parent. If there is calculable risk coming from both the sire and dam, then formulas must be used. The risk of being affected is one-half the sire's carrier risk times one-half the

dam's carrier risk. (Example from the pedigree: Half the sire's carrier risk is .0625 and half the dam's carrier risk is .0838, so the chance of producing an affected dog is .0625 x .0838 = .0052or 0.52%.)

Computing carrier risk depends on whether it is known if the dog or ancestor whose risk you are computing is affected or not. If it is not known whether the individual in the pedigree is affected, then the carrier risk is one-half the sire's carrier risk plus one-half the dam's carrier risk, minus the affected risk of the dog. From the prior example: .0625 + .0838 - .0052 = .1411 or 14.11% chance of being a carrier. If it is known that the dog is not affected, then there is a more complicated formula: (S + D - (2SD))/(1 - SD) where S = one-half the sire's carrier risk, and D = one-half the dam's carrier risk.



The goal of relative risk pedigree analysis is to plan matings below the average of the breeding population. This in turn will lower the carrier rate for the breed. Calculating and averaging the relative carrier risk of the breeding dogs in the population determines the average carrier risk. The use of the Hardy-Weinberg law to determine the average carrier risk of the population (based on the percentage of proven affected dogs) is not valid. It can only be applied to randomly bred populations, where there is no selection of breeding stock, and all offspring have an equal chance to produce the next generation.

Some breeders feel that all dogs with unknown carrier risk should be assigned the average risk of the breeding population; i.e., if it is estimated that 14% of the population are carriers, then anyone without computable risk will be assigned a risk of 14%. This is an incorrect use of relative risk analysis, as breeders would lose the ability to select matings below the breed average.

If a breeder has a quality dog with a higher than average relative risk, it can be bred to a mate with a low relative risk. A lower-risk offspring that exceeds the higher-risk parent in quality should replace the higher-risk parent in the breeding program. The number of breeding offspring from higher-risk parents should be limited, so that you avoid the possibility of multiplying a defective gene in the breeding population.

Relative risk assessments only take into account the identified carrier and affected individuals in the pedigree. Therefore, these estimates determine the *minimum* risk based on the information available. If additional affected relatives to the pedigree are diagnosed, the computed risk will rise. Pedigree analysis can never clear a dog of being a carrier. If there is no known risk behind a dog in the pedigree, the relative risk of the dog is not zero; it is unknown.

Relative risk pedigree analysis will select against whole families of dogs based on their relationship to known carrier and affected dogs. Therefore, genetically normal dogs will be selected against. However, for breeders with dogs at high risk of being carriers and no genetic test, it is the only tool that objectively allows them to lower the risk of their breeding stock and minimize the risk of producing affected dogs.