Using a Genetic Pedigree to Select Against Genetic Disease
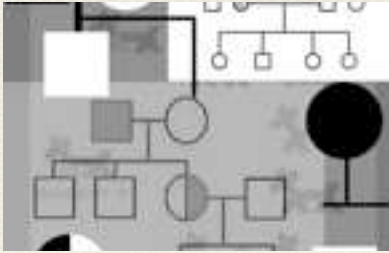
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Introduction

On the following three pages you'll find a short introduction to the basic concepts involved in using genetic pedigrees to help make the decision about whether or not to breed two dogs. Generally you would need to have two separate pedigrees, one for the possible dam and one for the possible sire. GDC creates genetic pedigrees using a program called Progeny, and uses data either from the GDC registries, or from information you supply from your own database. (A simple pedigree can be created from just a handful of dogs. Contact GDC for more details.

What is a genetic pedigree?

A genetic pedigree focuses on the relationships among dogs within 2-3 generations, and :

- shows the relationships among many dogs in a family group
- based on a particular dog of interest to a breeder or buyer
- helps you keep track of particular genetic traits and possible carriers
- can be expanded as you learn about and add more dogs
- typical size is 50-75 dogs

A traditional pedigree shows the parentage of a purebred dog back through three or more generations. If you take a traditional pedigree and begin filling in the rest of the close relatives (siblings, half-sibs, offspring, multiple matings, etc.), you've got the beginnings of a genetic pedigree (lets' call it a genped for short).

The genetic pedigree can be as simple or as complicated as you want, but the goal is to help you see the relationships among as many dogs as possible in a family group. If you are trying to select against a particular genetic disease, it is essential that you find out which dogs in the family group have been affected with the disease, and use that information to make estimates about the risk that any particular dog of interest to you has for being affected or a carrier.

A typical genped might include 50-75 dogs. Each dog is represented by a square (male) or circle (female). Lines drawn between dogs show that they have been mated, and lines descending from those mate lines show the litters they have produced. Your GDC/SIGHT genped will have a key explaining all symbols and text. Simple genpeds are easy to understand. Complex genpeds require some patience before you can make sense of the complicated relationships.

Ideally, each dog in the genped has been screened for at least one of the genetic diseases that you're trying to select against. But, in reality, you may have little or no information on most of the dogs. In addition, the genped may not show many key relationships if those dogs are not in the registry. For example, the sire of a dog you are interested in may have been breed to several other dams. The litters from those other dams may hold crucial information about whether or not the sire is a carrier. So the genped becomes more useful as you research and add missing pieces.

We create our genpeds with a program called Progeny (designed for human medical genetics work) which takes the information on a family of dogs from our registry or customer-supplied database and automatically draws the chart. Usually we will base the genped on a particular dog that a breeder is interested in. We then customize the chart to show the relationships involving that dog as clearly as possible. In extremely complex genpeds we may add a sub-pedigree or remove dogs in order to show the significant relationships more clearly.

Small genpeds can fit on a single 8.5x11 sheet of paper. Big genpeds are printed on several sheets of paper and then taped together.

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What is the purpose of a genetic pedigree?

- helps breeders select against one or more genetic diseases
- lowers the risk of producing affected or carrier dogs
- helps analyze the risk that any particular dog may be a carrier or affected
- identifies dogs or litters where more information is needed

The basis of a good breeding program is to select for the traits you want, and to select against the traits you don't want. If you choose a dam and a sire at random you'll tend to get a litter that's more or less the breed average of good and bad traits. But ideally you want to produce puppies with a higher than breed average set of good traits and a lower than average set of bad traits. All traits, of course, both good and bad, are the results of the genes a puppy inherits from its parents.

So a genped helps you to visualize the complicated relationships among dogs and to estimate the likelihood that any particular dog does, or doesn't, have the set of genes that influences a particular trait.

Many canine genetic diseases are caused by a key gene that is defective (recent research is showing that gene interactions are vastly more complex than we believed, and that the "one gene/one disease" concept is very simplistic). So your goal as a breeder is to find out as much as you can about which dogs in a genped are carrying, or have a certain risk of carrying, the key defective gene associated with a particular disease.

The genped is basically a way of organizing your knowledge about a family group of dogs. The most important knowledge you need to have about each dog is: 1) Which dogs is it closely related to? and 2) Is it carrying the genes associated with a particular genetic disease? As you work with a genped, you'll pencil in information on each dog as you learn more by talking with breeders, owners and researching extended pedigrees.

How do you use the genped?

- Identify as many affected dogs as possible
- Identify known carriers (parents and progeny of affected dogs)
- Identify 50%-risk carriers (parents and progeny of known carriers)
- Estimate carrier risks for particular key dogs and for litters from possible matings
- Consult with a genetic counselor about risks of producing carriers or affecteds for a particular mating

Most of the genetic diseases of concern to dog breeders and owners are recessive traits. In general that means both parents must be carrying one or more of the key defective genes for there to be any possibility of producing affected puppies. Many genetic diseases affecting dogs (like lens luxation) are associated primarily with a key defective gene. This key gene may be regulated in complicated ways by other genes, but in general, a dog with two copies of that gene is at very high risk for becoming affected. Other diseases, like hip dysplasia, involve a number of key genes which can combine in an individual to produce various forms of the disease (hip dysplasia, for example, ranges from mild to severe).

The genped can tell you only a few things for sure, but most of the information you will be dealing with is in the form of probabilities and risk estimates.

Step #1: Identify significant relationships in the genped

--fix yourself a pot of coffee or tea, take the cap off a fresh highlighter pen and get friendly with the genped. You can always print out fresh copies, so don't worry about spills or mistakes. Highlight all of the key lines of relationship through which genes could be passed along to the dog you are interested in. Use a second color to highlight relationships to common parents or grandparents, or other lines of relationship where a single dog's genes head for your dog from two, or more, separate directions.

--write down all the questions you have, all the notes or comments that come to mind, all the breeders or owners you know who may be able to provide more information about any key dogs.

--If you are considering mating two particular dogs, remember that the information you are looking for is some guesstimate of the probability that either dog is a carrier. If you are dealing with a late onset disease, and if either of these dogs is younger than the age of onset of the disease, then you are also interested in the probability that this dog might become affected. And you are also looking for a guesstimate of carrier or affected risk for the offspring of this mating.

Step #2 Identify all known affected dogs

Rationale: Assume that there are more affected dogs in the population than are reported in registries. If the disease you are interested in is late onset, assume that any young dog could still become affected. Identify a dog as affected only if you are certain that the diagnosis is based on the best screening test available. (GDC, SIGHT, and OFA/CHIC registries do not identify a dog as affected without written veterinary confirmation.) Hearsay information should always be suspect.

- do everything you can to find all the affected dogs in this family group. If you have access to a breed-wide pedigree database, get complete listings of offspring from all key dogs and make an attempt find out if there were any affecteds in any of those litters.

Step #3: identify known ("assumed" or "obligate") carriers

(These dogs are parents and offspring of affected dogs)

Rationale: According to the rules of classic Mendelian genetics for recessive traits, an affected dog must have two copies of the defective gene: one inherited from the dam and one from the sire. (**Note:** Current research suggests that genes do not always behave exactly according to the rules of classic genetics, but even so, breeders can make significant progress by following the rules.)

☒   for a recessive trait or disease that is primarily associated with one gene (autosomal recessive), there is a very high probability that both of the parents and all the offspring of an affected dog are carriers of one copy of the defective gene.

☒   for a recessive trait that is polygenic (associated with many genes), there is a reasonably high probability that both parents and all offspring will be carrying a significant number of the defective genes.

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Step #4: Identify all dogs with a 1:2 (50%) probability of being carriers

(These dogs are parents and offspring of known carriers)

Rationale: According to classic genetics, at least one of the parents of a known carrier is also a carrier. Therefore each parent of a known carrier has a 1:2 (50%) probability of also being a carrier. In addition, each offspring of a known carrier has a 1:2 (50%) probability of being a carrier. (**Note:** You may have read that 50% of the offspring of a carrier are carriers themselves. This is misleading because it suggests that if a carrier produces a litter of 8 dogs, exactly 4 will be carriers. However, like a flipped coin, each offspring of a carrier has an equal chance of being a carrier or not. If you flip a coin 8 times, you won't always get exactly four heads and four tails.)

☒   If a dog in your genped has a 1:2 chance of being a carrier, you should do everything possible to find if that dog has produced an affected, because then you will have positive identification of the dog as a carrier. Try to obtain progeny lists for that dog, and contact the breeder of each of the litters.

☒   Tracking down the offspring of each known carrier will give you another list of dogs with a 50% chance of being carriers themselves. If any of those dogs is closely related to the dog you are interested in, you must try to find out if any offspring (second generation from the known carrier) are affected, because, once again, you should try to identify all the known carriers in the genped.

Step #5: Analyze the carrier/ affected risk for a particular dam and sire and their litter

Rationale: *If you have identified affected dogs, carriers, or 50%-risk carriers directly related to the dam or sire you are interested in, you can use relatively simple probability calculations to give an estimate of risk. (Note: This type of analysis will have a wide margin of error, because as we've noted above, genes don't always follow the rules of classic genetics. But with no other available information, this risk analysis may at least help you make*

a breeding decision if all other factors are more or less equal.)

☒   If at all possible, we urge you to consult with a genetic counselor at this point, after you've gathered as much information as possible in your gen ped.

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