Collecting and utilizing phenotypic data to minimize disease: A breeder's practical guide

Rhonda Hovan

Since its inception in 1966, the OFA has been providing information intended to help breeders reduce the incidence of genetic disease in dogs. Most breeders have found this service to be very helpful, and have seen important improvements in the health of their dogs through the diligent use of OFA data.

Yet there remains a widespread lack of understanding regarding the optimal use of phenotypic information in breeding programs. As a result, many breeders have not taken full advantage of the information available, slowing their progress toward minimizing disease. The methods of collecting and analyzing phenotypic data presented here offer breeders the opportunity to dramatically decrease the incidence of genetic disease in their breeding programs to a level often significantly below that reported as a breed average by OFA and other statistical databases.

A Comparison of Genotypic Tests to Phenotypic Tests

In recent years, DNA tests for numerous canine diseases have been developed, and this progress is expected to continue. Where available, such tests offer breeders direct information about the genes that an individual tested dog can contribute to his or her offspring. DNA tests are an example of genotypic tests, and are the gold standard as tests for disease causing genes. Breeders can be confident that DNA tests will provide them with very accurate information, leaving little room for an unexpected appearance of the gene in offspring.

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However, DNA tests are not available for the majority of common canine diseases. Most tests intended to offer breeders health information about a dog's suitability for breeding, rely instead on an evaluation of the dog's physical status at the time of examination. These are called phenotypic tests, and include evaluations for hip and elbow dysplasia, many eye and cardiac diseases, patella and thyroid disease, and most current canine disease evaluations.

Fortunately for the dogs – but unfortunately for breeders attempting to reduce the incidence of disease – many harmful genes do not manifest as detectable disease during the prime breeding age of the dog, if ever. These dogs may appear normal, yet carry genes capable of causing disease. A number of types of gene actions can contribute to this confusion, for example: recessive genes, incomplete penetrance of the gene, variable expressivity of the gene, multiple genes involved in the disease, and even environmental influence on expression of the trait. Further, diseases that have a late age of onset such as certain eye and cardiac abnormalities, can result in normal phenotypes for a period of time, even when the disease gene is present.

In an attempt to compensate for these inherent flaws with common phenotypic tests, many breeders have long realized the importance of gathering test information on more than just the prospective sire and dam of a litter. Because standard pedigrees include only direct ancestors such as parents, grandparents, great-grandparents and so on, these are the relatives on which breeders usually focus when seeking additional health information. It is not uncommon for conscientious breeders to build pedigrees which are described as "three generations clear" for a disease, meaning that the sire and dam, the 4 grandparents, and the 8 great-grandparents have all tested phenotypically normal. Yet such breedings may produce less than satisfying results, as the disease genes may still be present, and affected offspring may still be produced.

Fortunately, there is an additional way of utilizing phenotypic test data which improves the likelihood of producing predictable results. It involves a different method of building pedigrees.

Vertical Pedigrees

Traditional pedigrees expand horizontally; that is, they are read from left to right with relatively few dogs appearing at the far left and increasing to the predominant number of ancestors listed to the right. Although the dogs to the left (the sire, dam, and grandparents) most directly impact the resulting offspring, there are only six of these contributing data on this type of pedigree. That is a small sampling of the relevant information that may actually be available. While many additional dogs are named on the right side of the page, these more distantly related dogs are less significant genetically than are those on the left.

A pedigree can also be constructed vertically, most easily using a three column format. A vertical pedigree of "Dog A" begins page left with Dog A and all of his full siblings (from one or more litters). The central column lists his sire and dam, and their full siblings; with the right column doing the same with the four grandparents. Clearly, vertical pedigrees can include many more first and second generation relatives than do traditional horizontal pedigrees.

The value of vertical pedigrees can be most fully appreciated through understanding an essential genetic principle that should correctly be the foundation of most complex breeding decisions. This principle is that full siblings are, on average, equally genetically similar to each other as they are to each of their parents. All of the littermates taken as a group represent various combinations of their parents' genes, and are good indicators of the *range of possibilities* that are likely to be passed on from any one of them. Likewise, phenotypic information about the aunts and uncles of a given dog, is equally as important as is that of the grandparents. Thus, dogs who do not even appear on traditional horizontal pedigrees, may be more significant genetically than are the more distant relatives who do. By overlooking these siblings, aunts, uncles, great-aunts, and great-uncles, the pertinent data base may be reduced by as much as four fold or more (the number of littermates for whom data might be available).

The broad data base that is accessible using vertical pedigree analysis gives breeders accurate information about any trait that cannot be tracked in a direct manner. Whenever multiple genes and/or other complex modes of inheritance are involved, a larger sampling will be more likely to contain enough individuals to indicate a pattern. Accuracy then, is dependent upon accumulating phenotypic information on as many of these direct and indirect relatives as possible.

A simple example should help illustrate how this works. Suppose that a breeder would like to compare two potential stud dogs, "A" and "B," with regard to their likelihood of producing normal hips. Written in standard horizontal form, their pedigrees with OFA hip status noted* are as follows:

		Paternal Gr-Sire "Fair"			**Paternal Gr-Sire "Fair"**
	Sire "Good"			**Sire "Good"**	
		Paternal Gr-Dam "Good"			**Paternal Gr-Dam "Good"**
Stud Dog A "Fair"			**Stud Dog B "Good"**		
		Maternal Gr-Sire "Good"			**Maternal Gr-Sire "Good"**
	Dam "Good"			**Dam "Good"**	
		Maternal Gr-Dam "Good"			**Maternal Gr-Dam "Good"**

OFA Fair is in **Blue** type; OFA Good is in **Black** type, OFA Excellent is in **Green** type; Dysplastic dogs are in {red} type with brackets.

On the surface, both of these pedigrees appear to be making progress toward reducing the incidence of hip dysplasia. All other factors being equal, the investigating breeder might be persuaded by his more favorable hip rating to choose Stud Dog B. Imagine the frustration, then, if several of the resulting pups develop hip dysplasia.

Now expand the two pedigrees vertically, and compare the data that is available in this format:

<table>
<tr><th>1st Generation</th><th>2nd Generation
(Parents, Aunts, Uncles)</th><th>3rd Generation
(Gr-parents, Gr-Aunts, Gr-Uncles)</th></tr>
<tr><td rowspan="4"><u>Stud Dog A</u> “Fair”
Sibs (7):
Fair
Fair
Good
Good
Good
Excellent</td><td rowspan="2"><u>Sire</u> “Good”
Sibs (8):
Fair
Fair
Good
Good</td><td><u>Paternal Grandsire</u> “Fair”
Sibs (6):
Good
Good</td></tr>
<tr><td><u>Paternal Granddam</u> “Good”
Sibs (8):
Good
{dysplastic}</td></tr>
<tr><td rowspan="2"><u>Dam</u> “Good”
Sibs (10):
Fair
Fair
Fair
Good
Excellent
{dysplastic}</td><td><u>Maternal Grandsire</u> “Good”
Sibs (?)</td></tr>
<tr><td><u>Maternal Granddam</u> “Good”
Sibs (9):
Good</td></tr>
<tr><td rowspan="4"><u>Stud Dog B</u> “Good”
Sibs (9):
Fair
Fair
Good
{dysplastic}
{dysplastic}
{dysplastic}
{dysplastic}</td><td rowspan="2"><u>Sire</u> “Good”
Sibs (7):
Fair
Good
Good
Good
{dysplastic}</td><td><u>Paternal Grandsire</u> “Fair”
Sibs (7):
Fair
Fair
Good
Good</td></tr>
<tr><td><u>Paternal Granddam</u> “Good”
Sibs (?)</td></tr>
<tr><td rowspan="2"><u>Dam</u> “Good”
Sibs (6):
Fair
Fair
{dysplastic}
{dysplastic}</td><td><u>Maternal Grandsire</u> “Good”
Sibs (10)
Fair
{dysplastic}
{dysplastic}
{dysplastic}</td></tr>
<tr><td><u>Maternal Granddam</u> “Good”
Sibs (6):
Fair
Good
Excellent</td></tr>
</table>

An evaluation of the vertical pedigree reveals that Stud Dog A comes from a litter with predominantly normal hips, and this is consistent also with his sire, dam, and their siblings. Thus, the r*ange of possibilities* in his genetic package heavily favors normal hips.

In contrast, Stud Dog B dog comes from a litter in which half of the dogs are normal, and the other half are dysplastic (with one unknown). Furthermore, this is a pattern which can be traced back through his dam and maternal grandsire. Thus, despite his own "good" rating, Stud Dog B's *range of possibilities* may include a higher likelihood of transmitting hip dysplasia. This pedigree is not demonstrating progress toward reducing the incidence of affected dogs.

Additional Factors to Consider In Evaluating Vertical Pedigrees

Of course, not all vertical pedigrees will be as clear-cut as in the previous example. Further, diseases other than hip dysplasia may require a different process of analysis. Two of the most important variables to examine are:

1) the frequency of the disease in the vertical pedigree as compared to the frequency of the disease in the breed population, and
2) the location of the affected individuals on the pedigree.

Frequency of the disease in the vertical pedigree as compared to the frequency of the disease in the breed population

Because of the larger number of individuals represented on vertical pedigrees, sometimes very few pedigrees will appear completely free of affected dogs, as might be found using the traditional format. As illustrated with the example of Stud Dog A, even respectable and desirable pedigrees often contain an occasional affected dog. Therefore, a realistic goal for breeders is to use those pedigrees which demonstrate a significantly lower rate of disease as compared to the general breed population.

Since the incidence of any given disease varies from one disease to another, and from one breed to another, such factors should be taken into consideration when evaluating pedigrees. For example, with less common diseases, using completely disease-free vertical pedigrees may be the only way to maintain a low rate of disease in the breed. Diseases with a moderate or high breed frequency are most effectively managed by selecting individuals whose vertical pedigrees contain a large amount of data, and few affected dogs.

The location of the affected individuals on the pedigree

Of course, in addition to how many affected dogs appear on a vertical pedigree, their location on the page must also be taken into consideration. Clearly, dogs appearing farther to the left on the page have a more direct genetic impact than do those appearing toward the right. Further, multiple affected dogs within a single location may be an important factor. Thus, Stud Dog A's pedigree, with 2 dysplastic relatives scattered among 28 total dogs, would generally be considered to be a strongly normal pedigree. Yet even if nothing else were known about Stud Dog B except that he has 4 dysplastic siblings, this pedigree should be excluded from most breeding programs. With four affected dogs focused in the column farthest to the left, this pedigree has disease genes concentrated in a very influential position.

Collecting Data for Vertical Pedigrees

In many breeds and for many diseases, it is recognized that the availability of vertical pedigree data currently may be limited. This is partially due to the historical lack of understanding of the importance of such information. Now, through its commitment to breeder education, OFA hopes to stimulate a new and steady improvement in results, using this method of building and analyzing vertical pedigrees. If breed clubs also begin to emphasize the value of such pedigrees to their membership, it is reasonable to anticipate much wider availability of this data in the near future.

However, all breeders are encouraged not to wait for future change within their breed, but rather to create that change within their own breeding programs. Significant improvements are possible even in a relatively brief period of time, using very achievable methods of collecting data.

Building A Personal Data Base

Both long term breeders, and new hobbyists, can build a useable data base in as little as one or two generations. The most immediate information can be collected retrospectively by seeking examination results on the siblings of dogs currently being considered for breeding. Where available, results on those dogs' aunts and uncles can also be gathered. While such data may be spotty, it is worth making the effort to contact owners and breeders of those siblings, aunts, and uncles. OFA's online database is also searchable by siblings, and may provide some additional information.

Perhaps more effective, however, is to begin building a data base of all future puppies that a breeding program produces. There are two very effective strategies which can be used in combination to facilitate this process.

Strategy 1

Beginning prior to the sale of a puppy, the breeder typically discusses with prospective buyers, health examinations that have been performed on the sire, dam, and other relatives. This is the ideal time to explain to the buyer that his new puppy will also have valuable information to contribute to the next generation of the breeding program. Just as the current buyer appreciates and trusts a breeder who is conscientious about health issues, so the buyer will understand that he has a role in helping the breeder make good decisions about future litters. The breeder should explain clearly what examinations are expected, at what ages these are performed, typical costs, and other factors such as convenience (local health screening clinics if available; or if any traveling may be required).

In breeds for which there are numerous, expensive, or very inconvenient genetic screening tests, breeders may need to compromise to keep those burdens at a level which would be acceptable to most reasonable buyers. In such cases, the breeder may choose to focus efforts toward the most common or most debilitating diseases in the breed, or those which have the greatest impact on the individual breeding program. Because of practical considerations, it may be necessary to request only certain specific health screening examinations; and have the flexibility to forego results on diseases of lower priority.

Nonetheless, while agreeable at the time of sale, some buyers are still reluctant to follow through when the time comes. These buyers can often be coaxed to participate by offers of assistance, such as the breeder taking the dog for the exam, or the breeder offering to groom the dog prior to the examination. For greater assurance of compliance, many breeders find it effective to take a refundable deposit at the time of sale. This may be set approximately equal to or slightly higher than the costs of the health examinations, so that the buyer has incentive to complete the testing. It is also helpful to include the request for health screening examinations in the written sales contract or guarantee.

Strategy 2

The factors which take the greatest toll on buyer compliance are elapsed time, and lack of contact with the breeder. In diseases such as hip dysplasia, for which final OFA clearances are not available until the dog is two years old, it may have been 18 months or more since the breeder last spoke with the owner of the puppy. Especially if all is going well with the pup, the buyer may no longer be as concerned with health issues as he was prior to the purchase. Further, buyers are more reluctant to leave a refundable deposit when the term of the deposit extends out nearly two years.

To overcome all of those issues, breeders are encouraged to take advantage of early preliminary examinations in diseases for which preliminary evaluations have a high percentage of accuracy. For example, OFA preliminary hip evaluations done on dogs at 3 to 6 months of age, have an overall reliability of 89.6% for dogs graded as normal, and 80.4% for dogs graded as dysplastic.[1] That is, nearly 90% of dogs graded normal at 3-6 months of age on OFA preliminary evaluations, remained normal at 2 year final evaluations; and about 80% of those diagnosed as dysplastic between 3-6 months of age, remained dysplastic as adults. These percentages are even higher for dogs who were graded as "Good" or "Excellent", and "Moderate" or "Severe." Most of the dogs whose 2 year evaluations differed between normal and abnormal as compared to their 3-6 month evaluations, were those who were graded "Fair," "Mild," or "Borderline" on their preliminary report. The status of such dogs can be determined with greater accuracy with increasing age, and when possible, even non-breeding dogs in those categories should be resubmitted as adults.

This high degree of reliability means that OFA preliminary hip evaluations can have great value for breeders constructing vertical pedigrees. Because of the probability that most of the puppies a breeder produces will never have final hip x-rays submitted for certification, the possibility of obtaining much of that otherwise lost data on preliminary examination is very attractive.

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A number of other factors also contribute to the concept that obtaining early preliminary hip x-rays is a nearly ideal plan for breeding programs. First, current vaccine protocol recommends the last puppy vaccination at approximately 3-1/2 to 4 months of age. Since presumably all pups will be going to the veterinarian for this vaccination, it is usually a very convenient time to schedule the preliminary hip x-ray. Further, most pups of this age do not need sedation or anesthetic to obtain good positioning, thereby reducing cost and perceived risk to the dog. This time frame is also well within the period that the breeder usually has the most contact and influence with the buyer. All of these considerations combine to produce excellent compliance, and thus build a much larger data base than most breeders are able to obtain with 2 year hip evaluations. This greatly increased volume of data more than compensates for the slightly decreased rate of accuracy of preliminary OFA hip evaluations.

Breeders using this recommended early preliminary method of data collection may also choose to follow certain other associated procedures. The breeder may request that each puppy owner send the x-rays to the breeder, rather than directly to OFA. This provides the breeder with the opportunity to evaluate the films for correct positioning;, and the breeder can then take advantage of OFA's reduced price for preliminary hip evaluations of littermates submitted together. OFA's preliminary evaluation service provides the important advantages of known accuracy and consistency of preliminary evaluations; and of a written report that is widely accepted among breeders nationwide. Please note, however, that even when littermates' x-rays are submitted together, the OFA reports will be released only to the owners or co-owners as represented on the accompanying information cards.

An additional and highly useful advantage for breeders obtaining early preliminary data, is that the information gathered from a relatively recent litter may be taken into consideration as part of the decision making process prior to breeding subsequent litters with the same or similar parentage. Particularly in the case of a bitch, genetic information about her offspring that is not available until they are two years of age, sometimes comes too late in her breeding career to influence decisions appropriately. Preliminary genetic screening permits breeders to use the information in a much more timely manner, amplifying its immediate value to the breeding program.

Beyond Disease

As breeders become familiar with evaluating dogs or potential breedings using vertical pedigrees, they will find that its principles can be applied equally well to many genetic characteristics other than disease. Any trait for which there is a complex mode of inheritance can be examined more successfully using vertical pedigrees, than using the traditional horizontal format. And in fact, most conformation and performance characteristics are ideal candidates for vertical pedigree analysis; because achieving correct balance, breed type, movement, and desired temperament clearly is an extremely complicated task!

Vertical pedigrees can assist breeders in identifying "families" that have a strong likelihood of producing highly desirable characteristics, or those families in which less desirable traits may predominate. Careful examination of vertical pedigree data can help breeders avoid one of the most common mistakes of many breeding programs. This is that breeders frequently select an individual dog who manifests excellence in certain characteristics, and bring that dog into a breeding program hoping to add or strengthen those characteristics in their lines. Although they may have given consideration to that dog's sire and dam, they often overlook the fact that the desired traits are weak or absent in the littermates. Unfortunately, a single "star" littermate is likely to produce exactly that: litters that may contain a promising individual, but among more ordinary, possibly disappointing siblings.

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Consistent, predictable qualities are typically produced only when vertical pedigrees demonstrate those qualities consistently. In the majority of cases, dogs who are known as "prepotent" are those dogs whose vertical pedigrees show strong evidence of this consistency. Therefore, high quality dogs whose siblings and aunts and uncles are of similar high quality and desirability, are the dogs who will contribute that quality and desirability most reliably to their own offspring. Contrary to some common beliefs, it is not necessary for a dog to be line-bred to be prepotent, providing there is strong consistency within its first and second generation vertical pedigree. Using vertical pedigree data to achieve consistency without linebreeding also provides breeders with the opportunity to maintain a richer and more vigorous gene pool within their breeding program.

A Dependable Breeding Philosophy

The concepts advocated herein are based on sound genetic principles, and are designed to help breeders manage many types of complicated real world breeding decisions. The OFA recognizes that most hobby and competition breeders have admirable intentions, but are faced with a challenging blend of art and science in which one of the most frustrating aspects is the seeming unpredictability of results. Vertical pedigree construction and analysis is a very powerful tool which can assist in reducing surprises and improving predictability. With this method, progress toward one's goals is usually more assured, and the risks of unexpected and potentially devastating disease is decreased. This technique can help breeders build a foundation which can become stronger and more dependable with every successive generation. By working closely together, OFA and the conscientious breeders who depend on its services, can continue to make significant strides toward protecting and advancing the health of dogs.

Rhonda Hovan is a breeder, exhibitor, and judge of Golden Retrievers, and serves on the Board of Directors of the OFA. As a canine health and genetics writer, she has won the Veterinary Information Network Health Education Award.

1 Corley EA, Keller GC, Lattimer JC, et al. Reliability of early radiographic evaluations for canine hip dysplasia obtained from the standard ventrodorsal radiographic projection. J Am Vet Med Assoc 1997; Vol 211, No. 9; 1142-1146.