

Genetic Testing and Counseling: A Trojan Horse for Dog and Cat Breeds?

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Disease-causing genes are searched for by researchers, and the resulting genetic tests are desired by breeders. Once a genetic test is available, it is a double-edged sword: Its use can enable breeders to improve a breed or devastate it.

Most dog and cat breeds have a closed stud book, which means that there is a finite amount of polymorphic genes and genetic diversity present. They can only lose genes, not gain them through selective breeding.

The primary reaction of a breeder discovering that their breeding stock carries a defective gene is to retire it from breeding. As researchers, we often recommend using a genetic test to eliminate carriers from breeding.

The widespread elimination of all carriers of a high frequency gene can place a strong negative pressure on a gene pool. This can act to; decrease the genetic diversity of the breed, cause a loss of other quality genes, and increase the frequency of other defective genes through genetic bottlenecks.

We know that most individuals carry some undesirable genes. The more genetic tests that are developed, the greater chance that a breeder will identify an undesirable gene in their breeding stock. Making breeding decisions based on a single testable gene is inappropriate. Any quality individual that would have been bred if it had tested normal should still be bred if it tests as a carrier.

Prospective breeding animals represent the quality of the gene pool. A genetic test that was designed to help a breed and its gene pool should not be used to devastate it. As more genetic tests are developed, the discarding of individuals based on single, testable genes further restricts the gene pool. We should be offering genetic counseling recommendations that eliminate defective genes, but maintains breed lines and genetic diversity.

The best way to utilize genetic tests is to breed quality carriers to normal-testing mates, and replace them with quality, non-carrier offspring. This prevents affected offspring, while maintaining breed lines and genetic diversity in the breed.

Genetic Counseling and Control of Genetic Disease

The primary goal of domestic animal breeding is to maintain and enhance the quality of the breed. This is well understood in livestock production breeding, but often overlooked in dog and cat breeding. Breeders must consider all relevant aspects, which may include various health issues, conformation, temperament, and working ability. Health and diversity issues are important, but they must coincide with, and not replace selection for quality.

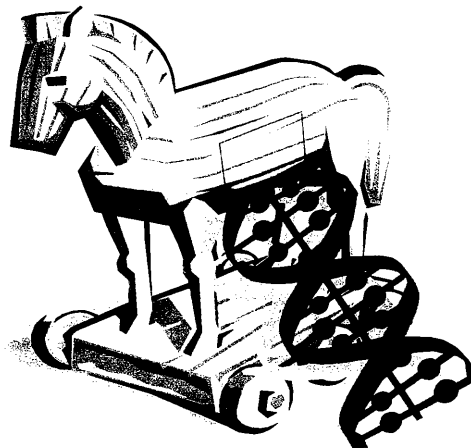
The goals of genetic counseling are to:

- 1) prevent the production of additional affected individuals
- 2) decrease the frequency of the defective gene(s)
- 3) maintain a genetically diverse pure-bred population

Genetic counseling recommendations need to take into account the dynamics and epidemiology of both the breed gene pool, and the defective gene(s). Rare or low frequency defective genes require more stringent selective pressure to prevent their spread. High frequency (breed-wide) defective genes require more pragmatic management that does not adversely affect the gene pool.

Genetic Counseling Recommendations

- Selection against a single gene trait with a test for carriers is based on the individual. Breeders only have to know the results of the individuals they plan on breeding.
- Selection against; disorders that lack a test for carriers, complexly inherited disorders, or disorders with an unknown mode of inheritance, require knowledge of the carrier or affected status of related animals.



Autosomal recessive disorders:

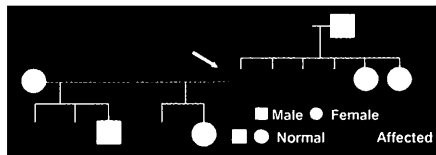
With a valid genetic test for carriers, breeders should mate quality carriers to normal-testing individuals, and replace the carrier parent with a quality, normal-testing offspring. Carrier-testing offspring should be selected against for breeding. In this way breeders can prevent affected offspring, while eliminating the defective gene from their breeding stock in one generation.

Without a genetic test for carriers, knowledge of the affected or carrier status of relatives is important. This requires testing for the affected phenotype, and knowledge of pedigree backgrounds. An **open health database** is the best method for objectively disseminating this information. Breeders should mate quality, higher-risk individuals to lower-risk individuals. Replace the higher-risk individuals with their lower-risk offspring. Repeat the process in the next generation. If the majority of breeders plan matings with a carrier-risk below the average of the breed, then the frequency of the defective gene will diminish in the population. This has been successfully done in many breeds. See **Relative Risk Pedigree Analysis** in the accompanying handout for a method to calculate relative risk.

In the Portuguese Water Dog, selection against the autosomal recessive gene for GM1-gangliosidosis (original carrier rate of 16%) resulted in the near elimination of the dominant ancestral line, and increased the frequency of prcd progressive retinal atrophy in the breed (resulting carrier rate of 35%).

X-linked (sex-linked) recessive disorders: Replacing affected and carrier individuals with normal male relatives will lose the defective gene in one generation. Avoid breeding high carrier-risk females, as half of the male offspring from carrier females will be affected.

Autosomal dominant and X-linked dominant disorders: Quality affected individuals should be replaced for breeding with a normal-testing parent, sibling, or prior-born offspring. Ideally you do not want to breed affected individuals, as half of their offspring will be affected.

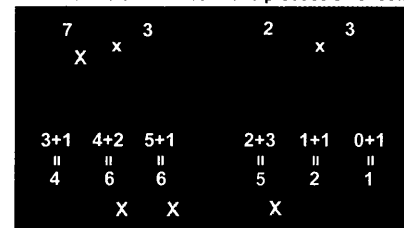


Genetic testing for the autosomal dominant genes causing polycystic kidney disease in Persian and Himalayan cats (38% affected worldwide) and hypertrophic cardiomyopathy in Maine Coon Cats (over 20% affected worldwide) will require careful selection to maintain breed diversity. Obviously, breeders do not want to produce additional affected cats. However, the wide scale elimination of 20% - 38% of a breed would put significant negative pressure on the gene pool – even in these populous breeds. The amount of quality genes and quality cats that can be lost forever from such selection, and the resulting genetic bottlenecks could be devastating.

Concurrently preserving the diversity of the gene pools over the next few generations, while at the same time eliminating the defective gene, is the most practical and desirable way to manage these disorders.

Complexly inherited (polygenic) disorders, and familial disorders with no known mode of inheritance: The knowledge of affected relatives is important in determining risk status. Open health database registries can provide this important information. Three factors should be considered:

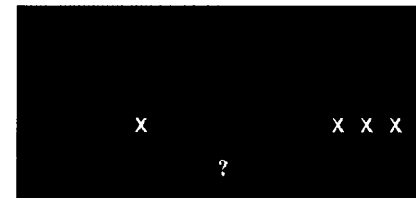
- 1) Complexly inherited disorders should be viewed as threshold traits. A number of genes must combine to cross a threshold to produce an affected individual.



- 2) Increased response to selection can be attained by attempting to break down the phenotype into measurable traits that may be more directly linked to the underlying genes.

Example: Measuring joint laxity, acetabular depth, or liability to secondary bony changes in hip dysplasia.

- 3) The most important method to manage complexly inherited disorders is to select for **breadth of pedigree normalcy**. Phenotypically normal individuals with normal or mostly normal littermates have the greatest chance of carrying normal genes. Phenotypically normal individuals with affected littermates have a greater chance of carrying a genetic load of disease-causing genes. Normal parents who have a preponderance of normal littermates provides even greater confidence. An open health database that shows genetic test results of close relatives can provide this information. See **CHIC – the Canine Health Information Center** in the accompanying handout.



Genetic tests are powerful tools, and as with any tool require an instruction manual for their proper use. When offering these tests to breeders, we need to provide genetic counseling advice that allows their use to be beneficial, and not detrimental to the breeds.



CHIC – the Canine Health Information Center

CHIC (www.caninehealthinfo.org) was established by the AKC Canine Health Foundation and the Orthopedic Foundation for Animals to assist breeds with managing breed-specific genetic disorders. The AKC national breed clubs determine the testable disorders for the breed (whether tests of the phenotype or the genotype).

Prospective breeding dogs can be researched, and their genetic test results, as well as that of their close relatives can be studied.

The benefit of the CHIC system is that dogs gain CHIC certification by completing their health testing, regardless of their test results. **CHIC is about health consciousness, not health perfection.** As more tests for defective genes are developed, every individual is likely to carry some deleterious genes.

BRAXFIELD FIRE POWER CHIC

Registration: SN71334501 Sire: SN35112001
 Breed: GORDON SETTER Dam: SN32439805
 Sex: M *Tries: CH
 Color: BLACK & TAN CHIC #: 14454
 Birthdate: Feb 4 2000 Addtl. Reg. #
 DNA Profile: V241451



Health Testing Results

Test Number	Step/Step	Report Date	Age	Result/Comments
GSE-3787F24M-PI	HIPS	Apr 9 2002	24	FAIR
	ELBOW	May 8 2002	24	UAP/DJO III UNILATERAL RIGHT
GSE-TH11/S1M-PI	THYROID	Jun 21 2004	S1	NORMAL

CHIC #/Name	Sex	Birthdate	Color	Relation	Test(s)	Result
MALCOLM BRAXFIELD BEMISIDE CHIC	F	Jan 29 1996		Dam	GSE-EL115F24-T GSE-498 GSE-3195G24F-T GSE-TH4/24F-T	
TIMBARY'S DANGEROUS LASSCH	M	May 10 1996		Sire	GSE-505 GSE-3280724M-T	
BRAXFIELD FIRE UP	F	Feb 4 2000		Full	GSE-EL198F28-PI GSE-3830E28F-PI GSE-TH15/32F-PI	
SHIRAZ'S MANDOLIN WIND	F	Jun 11 1999		Half(Sire)	GSE-EL196F34-PI	GSE-3816G34F-PI
SHIRAZ'S GO OUT DANCING	F	Jun 11 1999		Half(Sire)	GSE-EL200F37-PI	MODERATE
TIMBARY DANGEROUS ENCOUNTER	M	Jan 9 2000		Half(Sire)	GSE-585 GSE-3304F36M-PI	
MARLEENES RHYMA AT BEEACON	F	Jun 9 2000		Half(Sire)	GSE-624 GSE-3926F24M-PI	
MARLEENES SECRET AGENT MAN	M	Jun 9 2000		Half(Sire)	GSE-603 GSE-3837G24M-PI	
TIMBARY'S CLEARLY CLASSIC TARA	F	Nov 28 2000		Half(Sire)	MILD UNILATERAL LEFT	

Hip Status Vertical Pedigree

Printable Hips Elbows Cardiac Thyroid

TEALWOOD'S DESPITE ALL ODDS SN38210901

[Return to info display](#)

PEN OAK ROBERT E. LEE aka "GOOD" Sibs(2) GOOD(1) FAIR(1)	external grade(s) (?) SHANGRILA WYNDHIME paternal granddam "EXCELLENT" Sibs(0)
TEALWOOD'S DESPITE ALL ODDS subject "EXCELLENT" Sibs(2) GOOD(2)	QUAILFIELD MARK'S BUSINESS maternal granddam "GOOD" Sibs(4) EXCELLENT(1) GOOD(3)
Offspring(4) EXCELLENTE(1) GOOD(1) FAIR(1)	TEALWOOD'S HINE TO FIVE aka "GOOD" Sibs(3) GOOD(3)
	ORCHARD FARM DREAM GIRL maternal granddam "FAIR"

Relative Risk Pedigree Analysis

With simple autosomal recessive genes and no test for carriers, knowledge of affected and carrier relatives can provide an objective risk assessment. Relative risk is the **minimal risk** based on known risk from the pedigree. The following are obligate carrier risk values: Offspring of affected = 100%, Parent of affected = 100%, Phenotypically normal full-sib to affected = 67%, Full-sib to carrier = 50%.

If risk comes down from only one parent, then the offspring's carrier risk is half that of the parent. If risk comes down from both parents, then the **affected risk** is half the sire's risk times half the dam's risk.

S = risk of being carrier from the Sire.

D = risk of being carrier from the Dam.

Risk of being affected = S x D

The **carrier risk** depends on the knowledge of whether the individual can be excluded as phenotypically affected.

If you **do not know** if the individual is phenotypically normal or affected, then the risk of being a **carrier** is the sum of the risk from both parents, minus the risk of being affected.

Carrier Risk = S + D - (S x D)

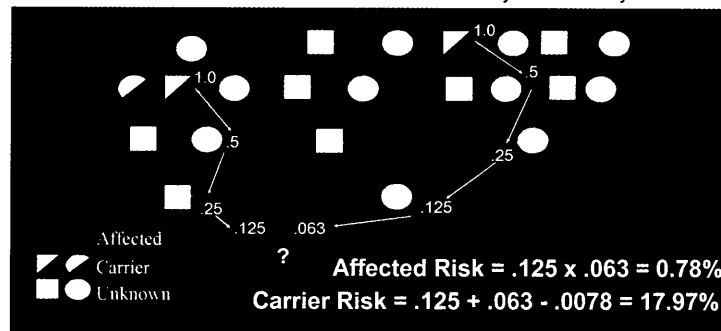
If affected individuals cannot reproduce, or it is **known** that the individual is not phenotypically affected, then:

$\frac{S + D - (2(S x D))}{1 - (S x D)}$

Carrier Risk =

Pros: Relative risk pedigree analysis objectifies risk relative to the population. It allows breeders to understand their own risk, and that of their proposed matings. It allows breeders with higher-risk breeding stock to lower their risk through planned matings.

Cons: Relative risk pedigree analysis selects against entire families, based on relatives with risk. It selects against both carrier and normal individuals. However, without carrier tests it is an effective tool to reduce the frequency of both affected and carrier individuals, and has been successfully used in many breeds.



A Few Words About Designer Breeds

There is a general misconception that mixed-breed dogs are inherently free of genetic disease. This may be true for rare, breed-related disorders; but the common genetic diseases that are seen across all breeds are seen with the same frequency in mixed-breeds. A mixed-breed dog with hip arthritis has no less a case of hip dysplasia than a pure-bred dog. Testing for inherited hypothyroidism (for thyroglobulin autoantibodies by Michigan State University) shows 11.5% of mixed-breed dogs to be affected (average for all breeds = 8.4%). Labradoodles are being diagnosed with hip dysplasia, elbow dysplasia, prcd-PRA, and inherited Addison's disease; all recognized disorders in both parent breeds. The most common inherited disorders for all breeds according to the AKC Canine Health Foundation are: cancer, eye disease, epilepsy, hip dysplasia, hypothyroidism, heart disease, autoimmune disease, allergies, patellar luxation, and renal dysplasia. With the exception of renal dysplasia, all of these conditions are routinely seen in mixed-breed dogs.

If the public is going to pay a premium for purposely-bred mixed-breed dogs; the only security that their pet may not develop genetic disease is if their parents were tested for the breed-specific genetic disorders. Their test results (or lack thereof) are viewable on the CHIC website.