Managing the Carriers – A Breed and Replace Strategy

PART II

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Gratitude Does Not Exist In Politics, Only In History

As discussed in Part I, breeders can use the Symbols Pedigree to map the inheritance of genetic traits from one generation to the next. It is useful because it collects information about all family members through successive generations including the cousins, aunts, uncles, grandparents and great grandparents. In this regard, it is the ideal pedigree for collecting and coding information in more depth. Its primary uses are to:

1. Identify carriers and specific traits of interest.
2. Code the carriers, affected and normals.
3. Locate the frequency of traits and disorders.
4. Highlight trends and/or patterns.
5. Aid breeders in the reduction of risk.

TEST MATINGS

Prior to the availability of DNA tests, breeders interested in knowing about the health and conformation of their dogs were forced to use test-matings in order to identify carriers. An individual being studied would be bred to a known (affected) animal and the progeny evaluated for the presence of a disease. If affected puppies were produced, the animal being studied would be evaluated to determine if it was a carrier. The following method was used to make that determination. If exactly five puppies are produced and only one is affected, the odds are 31 of 32 (about 87%) that the puppy in question is not a carrier. These odds are derived as follows: If the dog being tested is a carrier, each puppy has a 1 of 2 (50%) chance of being affected. If all five puppies are free of the disease, the probability that one will be an affected is $(1 \text{ of } 2)^5$ (i.e. one half raised to the fifth power) or 1 of 32 (Brewer, 2005). This method has several disadvantages. If the animal being evaluated is a carrier, the test-mating will produce affected pups which either must be euthanized or placed with owners willing to treat them.

With the exception of the genes on the X and Y chromosomes (sex chromosomes), genes come in pairs. Non-sex chromosomes are called autosomal and the paired genes on them are termed autosomal genes. Diseases caused by mutations in autosomal genes are classified according to whether one or two copies of the mutant gene are needed to produce a disease. If only one copy is needed to produce the disease and the other copy is normal, the result is a disease called autosomal dominant. If both copies of the gene must be mutant to cause a disease, the term used is called autosomal recessive (Brewer, 2005).

Some diseases are caused by autosomal recessives. The carriers of these diseases can be difficult to identify until a mating produces one or more affected offspring. What this means is that managing the carriers in some breeds will be more difficult than in others, in part because the number of carriers is often much higher than one would expect. For example, canine copper toxicosis (CT) in Bedlingtons Terriers is an autosomal recessive disease that causes copper accumulation and results in liver failure. Affected dogs become ill, and if untreated, generally die between 2 and 5 years of age. Because of its late onset, affected animals are often bred before being diagnosed. In Bedlingtons, 25% are affected, 50% are carriers and 25% are considered clear or normal (Brewer, 2005). Other breeds also have high carrier populations. A disease called von Willebrand's (bleeding disease) is considered prevalent in about 70% of Dobermans (Bell, 2002).

Once the Symbols Pedigree has been color coded a breeder can see where the carriers are located. This can lead to better selection and management of the carriers by retiring them using a breed and replace strategy. This approach assumes that quality offspring will be saved for future breedings. In order to minimize the number of quality dogs that are excluded from a breeding program, a technique called managing the carriers was developed. While no one answer fits every situation, there are useful guidelines that help manage the carriers, preserve breeding lines, maintain genetic diversity and reduce the risk of producing defects, unwanted traits or genetic diseases.

GUIDELINES

Autosomal Recessive Disorders.

These disorders are caused by a single recessive gene that is not sex-linked. If a test has been developed that will test for carriers (traits or diseases) the recommendation is to test the breeding stock and only breed to the carriers that are of quality that test normal. The goal should be to replace carriers with normal-testing offspring that are equal or better in quality then one or both of their parents. This approach allows breeders to save the good genes that took generations to collect. This is called a breed and replace strategy. If no test is available, the breeder must decide if the qualities seen in the animal being studied are sufficiently high enough to include it in a breeding. This requires information to be collected on the littermates of the immediate ancestors (14).

Autosomal Dominant Disorders

Unlike autosomal recessive disorders, these diseases are less troublesome to manage because each affected animal has at least one affected parent. One of the problems a breeder will encounter is that an autosomal dominant disorder is often not discovered until after breeding age (late onset). A few examples of late-onset diseases in dogs include cataracts, epilepsy and hip dysplasia. Whether they are dominant diseases is unknown. However, if a genetic test is available, breeding stock should be tested. Those that test positive should be excluded from breeding.

If the disorder falls into the broader category known as the dreaded diseases, which means those that kill, cripple, cause blindness or early death, the recommendation is to not breed these dogs to individuals that are affected. Another problem that breeders will experience when trying to control the carriers is called incomplete penetrance. In other words, some individuals will not show the disorder and roughly half of their offspring will be affected (Bell, 2007).

Sex-linked Disorders

Sometimes called X-linked, these disorders can be managed by tracing the ancestors in a pedigree. If a male is affected, he would have received the defective gene from his carrier mother. All of his daughters will be carriers, but none of his sons. If an affected female is bred, all of her sons will be affected and all of her daughters will be carriers. The recommendation for managing these individuals is to follow the same breed and replace recommendation outlined above for autosomal recessive disorders. There are rare instances when a female is affected. In these instances she will have received the defective gene from both of her parents.

Polygenic Disorders

These disorders are the most difficult to control and manage because they are caused by more than one pair of genes, and those that are affected are not necessarily affected by the same combination of genes. For most of the traits and disorders caused by polygenes no test has been developed. The problem in developing tests for these disorders is the number and combination of genes involved. One example of a polygenic disorder for which no test has been developed is hip dysplasia (HD). It occurs in many breeds and has been a problem for breeders since it was first reported in 1935. What further complicates a solution for this disorder is the number of genes involved and the fact that the genes for the right and the left hip and the genes for the right and the left femoral heads might be different genes. Therefore a simple solution is not likely. The Orthopedic Foundation of America (OFA) (Keller, 2007) recommends the following:

- Breed normal to normal.
- Breed normal dogs that come from normal parents and grandparents.
- Breed normal dogs that have more than 75% normal siblings.
- Select dogs that have a record of producing a higher than breed average percentage of normal progeny.
- Choose replacement animals that exceed the breed average.

CONCLUSION

In the final analysis, there are more than enough problems to worry about in each breed. Therefore, the time and effort spent on collecting and studying pedigrees for wanted and unwanted traits should be given a high priority. Breeders will always have the opportunity to study the rare and suspected problems in their breed, but they must always give the dreaded diseases (defined above) more attention than other disorders.

In order to manage the carriers, breeders must be disciplined in their efforts as they collect and analyze information. More importantly, they must be thoughtful in the ways they use the resultant offspring they produce because some will have carriers in their pedigrees. These efforts can be time consuming and tiring, but in the end it is well worth it. Listed below are the DNA tests for each disorder and the breeds for which a test exists. Contact information for the laboratories that conduct the tests is also listed.

CONTACT LABORATORY SOURCES:

Alfort School of Veterinary Medicine: France, http://www.labradorcnm.com/ Animal Helath Trust: (England): http://www.aht.org.uk/sci_disc_genetics_dna.html#canine

Auburn University – Boudreaux Lab: http://www.vetmed.auburn.edu/index.pl/Boudreaux_mk (334) 844 2692

Cornell – Goldstein Lab.: http://www.vet.cornell.edu/labgoldstein/ (607) 253 4480 Cornell Univ. Comparative Coagulation Lab. http://www.diaglab.vet.cornell.edu/coag/test/hemopwh.asp (607) 275 0622

GenMark: http://www.genmarkag.com/home_companion.php (877) 766 3446

Health Gene: www.hearthgene.com (877) 371 1551 Jefferson Medical College: David.wenger@mail.tju.edu

Michigan State University – Peterson-Jones Lab: http://www.cardigancorgis.com/PraPressRelease.aspx (517) 353 3278

New York University Neurogenetics lab: http://pwdca.org/GM1app.html (212) 263 2943 Optigen: www.optigen.com (607) 257 0301

PennGen: www.vet.upenn.edu/penngen (215) 898 8894

UC Davis – Lyons Lab: http://www.vgl.ucdavis.edu/service/catPKD.html (530) 752 2211

U Missouri – Johnson Lab: http://www.caninegeneticsdiseases.net/ (573) 884 3712 U New South Wales- Wilton Lab: a.wilton@unsw.edu.au

U Florida – Neuro Service: http://www.neuro.vetmeded.ufl.edu/dm_flash_test_web/index.html (352) 392 4700 x 4700

VetGen: www.vetgen.com (800) 483 8436

Washington State U – Meurs Lab: http://www.vetmed.wsu.edu.edu/deptsVCGL/ (509) 335 6038

Washington State U – Pham Lab: http://www.vetmed.wsu.edu.edu/annonements/invermectin/ownerinfo.asp (509) 335 3745

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Bell, J., 2007. Breeding Strategies for the management of genetic disorders. The Hydrant, Aug., pp. 8-9.

Bell, J., (2000) Choosing wisely, American Kennel Club, Gazette, New York, NY., Aug., Vol. 117, Number 8, p. 51.

Keller, G., 2007. The use of health databases and selective breeding. Orthopedic Foundation of America, St Louis, Mo.

Brewer, G., 2005. Canine molecular genetic disease. Proceedings, Tufts' canine and feline breeding and genetics conference, Sept., 30-Oct., 1, Sturbridge, MA.

ABOUT THE AUTHOR

Carmen L. Battaglia holds a Ph.D. and Masters Degree from Florida State University. He is an author of many articles and several books, an AKC judge, researcher, well known breeder and lecturer on the breeding of better dogs. For more information about his writings go to: www.breedingbetterdogs.com

CANINE GENETIC TESTS

DISORDER	BREED	TEST TYPE	TEST ORG.
Canine Leukocyte Adhesion Deficiency (CLAD)	Irish Red & White Setter Irish Setter	Direct	Optigen
Cataract, juvenile (Early onset Hereditary Cataract – EHD)	Boston Terrier French Bulldog Staffordshire Bull Terrier	Direct	Optigen
Ceroid lipofuscinosis	Border Collie	Direct	Optigen
Ceroid lipofuscinosis	American Bulldog Dachshund England Setter	Direct	U Missouri
Coat Color and Nose Color variations	Australian Shepherd Border Collie Brittany Belgian Shepherd Belgian Tervuren Cardigan Welsh Corgi Collie (Rough, Smooth) Cocker Spaniel Curly-Coated Retriever Belgian Malinois Dachshund Dalmatian Doberman Pinscher English Cocker Spaniel Engish Setter English Springer Spaniel Field Spaniel Flat-coated Retriever French Bulldog German Shepherd Dog German long haired Pointer German Wirehaired Pointer Great Dane Greyhound Groenendael Labrador Retriever Laekenois Large Munsteriander Lowchen Newfoundland Pointer Pomeranian Poodle Portuguese Water Dog Pudelpointer Shetland Sheepdog Staffordshire Bull Terrier	Direct	HealthGene

DISORDER	BREED	TEST TYPE	TEST ORG.
	Whippet Wirehaired Pointing Griffon		
Coat Color Gene Variations	Alaskan Klee Kai American Cocker Spaniel Australian Cattle Dog Border Collie Curly Coated Retriever Dalmatian Doberman Pinscher English Cocker Spaniel English Springer Spaniel Flat Coated Retriever Gordon Setter Labrador Retriever Newfoundland Pointer Poodle Schipperke Scottish Terrier Stumpy Tail Cattle Dog	Direct	
Coat Length (FGF 5)	Weimeraner	Direct	Animal Health Trust
Cobalamin Malabsorption (Methylmalonic Aciduria)	Australian Shepherd Giant Schnauzer	Direct	PennGen
Collie Eye Anomaly (Choroidal Hypoplasia)	Australian Shepherd Border Collie Lancashire Heeler Nova Scotia Duck Tolling Retriever Rough Coated Collie Shetland Sheepdog Smooth Coated Collie Whippet Longhair	Direct	Optigen
Cobalamin Malabsorption (Methylmalonic Aciduria)	Beagle Border Collie DSH Shar Pei	Phenotypic	Penn Gen
Cone (Retinal) Degeneration	German Shorthaired pointer	Direct	Optigen
Congenital Hopothyroidism With Goiter (CHG)	Rat Terrier Toy Fox Terrier	Direct	Michigan State U. Fyfe Lab PennGen

DISORDER	BREED	TEST TYPE	TEST ORG.
Congenital Stationary Night Blindness (RPE65-CSNB)	Briard	Direct	Optigen Animal Health Trust
Cystinuria	Newfoundland Labrador Retriever	Direct	Optigen (Newf only) PennGen VetGen (Newf only)
Degenerative myelopathy (DM)	German Shepherd Dog (Flash test) Boxer (RAPD) Pembroke Welsh Corgi (RAPD) Rhodesian Ridgeback (RAPD)	Direct (Suscept-ibility loci)	U-Florida – Neuro Service
Factor VII Deficiency	Alaskan Klee Kai Beale Scottish Deerhound	Direct	PennGen
Factor IX Deficiency	Kerry Blue Terrier	Direct	PennGen
Fanconi Syndrome	Basenji	Linked Marker	U-Missouri
Fanconi Syndrome	Basenji Norwegian Elkhound	Phenotypic	PennGen
Fucosidosis	English Springer Spaniel	Direct	PennGen Animal Health Trust
Glanzmann's Thrombasthenia (Type I)	Great Pyrenees Otterhound	Direct	Auburn U – Boudreaux Lab
Globoid cell Leukodystrophy	Cairn Terrier West Highland White Terrier	Direct	Jefferson Medical College
Glycogenosis (GSD) Type IIIa	Curly Coated Retriever	Direct	Mich. State U Fyfe Lab
Glycogenosis (GSD) Type IV	Norwegian Forest Cat	Direct	PennGen
GM1-Gangliosidosis	GM1-Gangliosidosis	Direct	NY U, Neuro-genetics Lab
Hypertrophic Cardiomyopathy	Maine Coon Cat Ragdoll	Direct	Washington State U., Meurs Lab
Ivermectin Sensitivity (MDR-1)	Australian Shepherd Collie Old English Sheepdog Shetland Sheepdog	Direct	Washington State U., Pharm Lab
L-2-HGA (L-2-hydroxyglutaric aciduria)	Staffordshire Bull Terrier	Direct	Animal Health Trust
Mannosidosis	DSH Persian	Direct	PennGen

DISORDER	BREED	TEST TYPE	TEST ORG.
PennGen	Australian Shepherds Beauceron Shepherd Border Collie CArdian Welsh Corgi Catahoula Leopard Dog Chihuahua Cocker Spaniel Collie Dachshund Great Danes Norwegian Hound Pitt Bull Pomeranian Pyrenean Shepherd Shetland Sheepdogs	Direct	GenMark
Mucolipidosis II (I-Cell Disease)	DSH	Direct	PennGen
Mucopoly-saccaharidosis (MPS)	DSH German Shepherd Dog Miniature Pinscher Miniature Schnauzer Schipperke Siamese	Direct	PennGen
Muscular Myopathy (Centronuculear Myopathy)	Labrador Retriever	Direct	Alfort School of Vet Medicine, France
Myotonia Congenita	Miniature Schnauzer	Direct	Optigen PennGen
Narcolepsy	Dachshund Doberman Pinscher Labrador Retriever	Direct	Optigen
Neonatal Encephalopathy	Standard Poodle	Direct	U Missouri
Neophropathy (Hereditary N., Familial N.)	English Cocker Spaniel	Direct	Optigen
Phosphofructo-kinase Deficiency (PFK)	American Cocker Spaniel English Springer Spaniel	Direct	Optigen PennGen VetGen Animal Health Trust
Polycystic Kidney Disease (PKD)	American Shorthair Himalayan Persian Scottish Fold	Direct	UC-Davis – Lyons Lab. Animal Health Trust
Primary Hyperpara-thyroidism	Keeshond	Linkage	Cornell – Goldstein Lab.

DISORDER	BREED	TEST TYPE	TEST ORG.
Progressive Retinal Atrophy (cord1)	Dachshund, Miniature Longhaired English Springer Spaniel	Direct	Animal Health Trust U Missouri
Progressive Retinal Atrophy Dominant	Bullmastiff English Mastiff	Direct	Optigen
Progressive Retinal Atrophy (prcd)	American Cocker Spaniel American Eskimo Dog Australian Cattle Dog Chesapeake Bay Retriever Chinese Crested Cockapoo English Cocker Spaniel Entelbucher Mt. Dog Finnish Lapphund Golden Retriever Kuvasz Labradoodle Labrador retriever Lapponian Herder Nova Scotia Duck Trolling Retriever Poodle (miniature, toy) Portuguese Water Dog Spanish Water Dog Stumpy Tail Cattle Dog Swedish Lapphund	Direct	Optigen
Progressive Retinal Atrophy (rcd1)	Irish Red & White Setter Irish Setter	Direct	Optigen Animal Health Trust
Progressive Retinal Atrophy (rcd3)	Cardigan Welsh Corgi	Direct	Mich. State U. - Peterson-Jones Lab. Optigen VetGen
Progressive Retinal Atrophy (rcd1a)	Sloughi	Direct	VetGen (Irish Setter)
Progressive Retinal Atrophy – Type A	Miniature Schnauzer	Direct	Optigen
Progressive Retinal Atrophy – X-Linked	Samoyed Siberian Husky	Direct	Optigen

DISORDER	BREED	TEST TYPE	TEST ORG.
Pyruvate Dehydrogenase Phosphatase Deficiency (PDH or PDP 1)	Clumber Spaniel Sussex Spaniel	Direct	U Missouri Animal Health Trust
Pyruvate Kinase Deficiency (PK)	Abyssinian American Eskimo Dog Basenji Beagle Cairn Terrier Chihuahua Dachshund DSH Somali West highland White Terrier	Direct	Optigen (Basenji) PennGen (All) VetGen (Basenji) Animal Health Trust (Westies)
Renal Dysplasia	Lhasa Apso Shih Tzu Soft Coated Wheaten Terrier	Linkage	VetGen
Retinal Dysplasia – Canine Multi-focal retinopathy (CMR)	Bullmastiff Coton de Tulear Dogue de Bordeaux Great Pyrenees Mastiff (English & French)	Direct	Optigen
Severe Dysplasia – Canine Multi-focal Retinopahty (CMR)	Bullmastiff Coton de Tulear Dogue de Bordeaux Great Pyrenees Mastiff (English & French)	Direct	PennGen
Severe Muscular Atrophy	Maine Coon Cat	Direct	Michigan State U – Fyfe Lab.
Thrombopathia	Bassett Hound Landseer Sptiz	Direct	Auburn U – Boudreaux Lab.
Trapped Neutrophil Syndrome (TNS)	Border Collie	Linkage	U. New South Wales
Von Willibrand's Diesase	Bernese Mt Dog Doberman Pinscher Drentsche Patrijshound German Pinscher Kerry Blue Terrier Manchester Terrier Papillion Pembroke Welsh Corgi Poodle Scottish Terrier Shetland Sheepdog	Direct	VetGen
Von Willibrand's Diesase	Irish Red & White Setter	Direct	Animal Health Trust