

**AUSTRALIAN TERRIER CLUB OF AMERICA  
NATIONAL PARENT CLUB HEALTH CONFERENCE**

**ST. LOUIS, MISSOURI**

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**By William I. Christensen, MD, MPH**



Friday afternoon's session became with a presentation on the emerging realization of the importance of the intestinal microbiota (population of micro-organisms residing in the gut) and ending with a hoped-for role of cannabidiol oil in treating drug-resistant epilepsy

Jan S. Suchodolski, DrMedVet, PhD, DACVM, AGAF, Associate Professor and Associate Director of the GI lab at Texas A & M University, discussed: "New Approaches to Diagnosis and Therapy of Intestinal Microbiota Dysbiosis." Traditional bacteriology cultures vastly underestimate the numbers of microbes residing in our guts since most of these organisms are strict anaerobes and will not grow in atmospheres where oxygen is present. This has resulted in an overemphasis, from a population standpoint, on *E. coli* and on the pathogenic bacteria which have been traditionally cultured in order to diagnose human bacterial infections. *E. coli* accounts for less than 1% of the gut flora. Newer PCR-based analyses give a more accurate representation and have allowed for the calculation of a "dysbiosis index," by counting the relative number of 8 bacterial types. Although the distribution of bacterial types varies greatly from individual to individual, it is relatively constant for each. However, some diseases and the administration of antibiotics greatly disrupt this population, a condition called "dysbiosis."

In gastrointestinal diseases, the normal mucous layer lining the intestines becomes thinned or disappears and the connections between mucosal lining cells less tight. Intestinal bacteria reside adjacent to or interposed with intestinal cells, which greatly disrupts the normal digestion and metabolism of carbohydrates, lipids, amino acids, nucleotides, xenobiotics and vitamins. For example, bile acids, which are produced by the liver and excreted in the bile, are important nutritionally, and 95% are normally reabsorbed by the small intestine and act as "regulators" of other organ systems, which may be disrupted if reabsorption is abnormal. In response, the liver may produce more bile acids, causing further harmful effects. For example, the proper development of puppies depends on the growth of *C. difficile* in the gut, which is controlled by the level of bile acids.

The use of certain antibiotics may greatly disrupt the normal gut biome. Dr. Suchodolski's research has shown that the effect of metronidazole, an antibiotic traditionally used to treat acute canine diarrhea, produces a marked change in the gut flora. If continued long enough, a normal distribution of types of bacteria never returns. In humans this change has been associated with the later appearance of Crohn's Disease but not ulcerative colitis and may be associated with the development of other immunologic disease such as asthma.

New studies in dogs have revealed that the use of antibiotics in acute diarrhea is ineffective in treating the diarrhea but does result in the appearance of antibiotic-resistant *E. coli*. “Fecal microbial transplantation,” (fecal enemas with feces derived from normal dogs) will result in short-term restoration of a normal gut biome in dogs who have developed an abnormal gut flora, but this effect may not be persistent if there is an underlying inflammatory condition of the intestine. (The use of fecal microbiota transplantation in dogs derives from its effectiveness in treating refractory or recurrent *C. difficile* infections in humans although this type of infection has not been reported in dogs or in cats. (In humans “poop pills” rather than enemas are used to establish a more normal flora.)

Dr. Suchodolski’s emphasis was on the interdependence of the gut flora and its human host. Whatever affects one, affects the other. Almost every disease is somehow associated with changes in the gastrointestinal microbiota.

The next presentation, by Michael Lappin, DVM, PhD, DACVIM (Small Animal Internal Medicine), Professor in Small Animal Clinical Veterinary Medicine at Colorado State University, concerned the use of probiotics in managing gastrointestinal diseases, especially acute or chronic diarrhea due to infectious diseases, but also in mitigating antibiotic-associated vomiting or diarrhea, and perhaps also useful in the treatment of inflammatory bowel disease although he did not discuss the last condition. He pointed out that all probiotics are not the same and that the choice of one should be based on the available scientific studies for that microorganism. He also pointed out that the organism in the product must still be alive in order to be effective. It is unknown whether the use of more than one different organism may be better than just one. Most of his work has been with FortiFlora, containing the probiotic strain *Enterococcus faecium* (SF68), produced and marketed by Purina for the dietary management of puppies and adult dogs with diarrhea and concerning which scientific studies have been done which would support its use. Since the organism is resistant to metronidazole, this antibiotic may be used in conjunction with FortiFlora. His research in cats has shown that the combination of this probiotic and metronidazole are more effective in the treatment of stress-induced diarrhea than the use of metronidazole alone. The importance of diet in causing diarrhea was demonstrated in one of his studies on shelter dogs, where the introduction of a standard diet, without either probiotics or antibiotics, resulted in a decrease in the incidence of diarrhea from 15% to 3%. He found in a study of the effect of amoxicillin/clavulanate (Clavamox) on cats that 23/27 cats developed diarrhea but that if FortiFlora were given first, the incidence of diarrhea greatly decreased.

He emphasized that all probiotics were not the same. Some probiotics can be immune modulators. For example, probiotic VSL #3 seems to help in inflammatory bowel disease in humans. In feline herpesvirus-1, (FHV-1), Dr. Lappin found that FortiFlora (SF68) significantly reduced the incidence of reactivation of the virus caused by stress. SF68 seems to work by activating T helper cells.

A presentation by Ragen T.S. McGowan, PhD, followed. Dr. McGowan is a Research Scientist in Behavior and Welfare at Nestle Purina. She asserted that: "There is mounting evidence that manipulation of the gut microbiota can influence anxious behavior, specifically via the gut-brain axis. She presented her research which showed that the use of *Bifidobacterium longum* (BL999), which is marketed by Purina as Calming Care, as a dietary supplement reduced such anxious canine behaviors as barking, spinning and pacing. Dogs also had reduced salivary cortisol concentrations in response to both exercise and anxiety-inducing stimuli when supplemented with BL999.

A presentation by Darcy Adin, DVM, DACVIM (Cardiology), Clinical Associate Professor of Cardiology at the University of Florida College of Veterinary Medicine, focused on the investigation of diuretic treatments and neurohormonal modulation of congestive heart failure. She noted that salt retention is a significant component of heart failure and that the worse the heart failure, the greater the sodium retention. She demonstrated that a low level of serum chloride, which she labelled "the forgotten ion," correlated well with severe heart failure. She discussed the drawbacks of furosemide (Lasix), which include variable absorption, especially if given with food, and suggested that torsemide ((Demadex) might be a better drug. Since low potassium also has an adverse effect in heart failure, she suggested that supplementation with potassium chloride (which has been used for many years) might be helpful.

Dr. Adin suggested that not enough emphasis was being placed on the role of nutrition in progressive heart disease and recommended a careful dietary history. Salt intake may be difficult to control in dogs because they dislike unsalted food and because many dog treats are high in sodium. She mentioned the probable role of taurine deficiency in at least some dogs with dilated cardiomyopathy (DCM). L-carnitine, another amino acid, may also be important in maintaining cardiac muscle, but, unlike taurine, blood levels do not reflect its presence since it is found primarily within cardiac muscle. However, like taurine, it seems to be a "benign" supplement. Coenzyme Q10, also known as ubiquinone-10 is a coenzyme important for cardiac metabolism and an antioxidant. She stated that: "It is probably benign." Omega-3 fatty acids, especially EPA and DHA had an anti-arrhythmic effect on the heart and seemed to improve muscle mass in cardiac cachexia (the loss of appetite associated with severe heart failure).

Stephanie McGrath, DVM, MS, DACVIM (Neurology) gave the final presentation of the afternoon. She discussed the inadequacy of currently available anticonvulsants in dogs (30% treatment failure) and the very limited human data which suggested that hemp-derived CBD oil (cannabidiol) might be helpful. She described her work identifying a reliable source of the oil and the pharmacokinetics of the agent. She is currently working on a double-blind, placebo,

cross-over trial which will eventually include 60 client dogs with intractable epilepsy. All dogs will have a spinal puncture and a brain MRI to rule out causes of seizures other than epilepsy. 4.5 mg/kg of CBD oil twice daily will be used. The AKC/CHF has fully funded this important research project.

Saturday morning's session began with a brief up-date on the Canine Health Information Program by Eddie Dziuk, MBA, COO of the OFA. He reminded the audience that CHIC was implemented by OFA and AKC/CHF in 2001 with 8 breeds participating. Now, over 180 breeds participate and 135,000 dogs have earned their CHIC numbers. 198 breeds have submitted DNA samples (cheek swabs and blood). He stated that DNA is extracted from the blood and stored frozen at the University of Missouri, Columbia. Cheek swabs are stored by University of California, Davis. He asked that owners who had previously submitted these samples update the clinical information on those dogs whose samples have been submitted by sending emails to [OFA@OFFA.ORG](mailto:OFA@OFFA.ORG) email text should include the dog's name and CHIC number, updated diagnoses, and associated documents such path reports. In this way the OFA can identify samples which might be pertinent to the work of a research scientist.

Steven Friedenber, DVM, PhD, DACVECC, Assistant Professor, Department of Veterinary Clinical Sciences, University of Minnesota, presented his work on the genetic basis for Addison's Disease in dogs. Addison's Disease is an autoimmune endocrine disorder in which the body attacks and destroys the outer layer of the adrenal gland, the adrenal cortex. Dogs with Addison's Disease are at high risk of developing a potentially deadly adrenal crisis characterized by shock, vomiting and life-threatening electrolyte abnormalities and not infrequently present in this manner to veterinary emergency facilities. In these cases, severe hypovolemic shock and elevated serum potassium levels are present, and the dogs may have heart rates of 30-40. Successful management of the disease is possible but requires lifelong hormone supplementation and careful monitoring. Addison's Disease primarily affects younger dogs. Standard Poodles, Portuguese Water Dogs, Bearded Collies, and Cocker Spaniels are among those breeds believed to have a genetic basis. A similar syndrome exists in humans, where those of Scandinavian descent are more affected. John F. Kennedy was affected by the disease.

The goals of Dr. Friedenber's research are to understand the genetics and immunology of the disease and, if possible, to develop a marker which would predict which dogs are at risk. An abnormality in Chromosome 37 has been identified and is present in 25% of affected dogs. It seems to be a complex genetic trait, and Dr. Friedenber is now doing whole genome sequencing to identify the causative mutation(s). He is also working on developing immunological assays for the autoantibodies present in young dogs destined to develop Addison's Disease and which will thus serve as a predictive clinical test.

Karen Muñana, DVM, MS, DACVIM (Neurology), Professor of Neurology at North Carolina State University College of Veterinary Medicine, presented the results of a retrospective study of 61 dogs presenting to NC State Veterinary Hospital between 2003-2017 (n=32) or identified in an AKC/CHF survey (n=29) with steroid response meningitis-arteritis (SRMA). She was interested in identifying the clinical features of the disease in this country as most of the previous studies were performed in Europe. SRMA is a common inflammatory disease of the nervous system of dogs characterized by involvement of the meninges (the membranes that cover the brain and spinal cord) and associated blood vessels. The cause is not understood but is believed to be immune-mediated. It typically affects dogs 6-18 months old. Any breed can develop the disease, but there seems to be a predisposition in Beagles, Bernese Mountain Dogs, Border Collies, Boxers, English Springer Spaniels, Russell Terriers, Nova Scotia Duck Tolling Retrievers, Weimaraners and Whippets. Diagnosis is based on the presence of increased numbers of neutrophils in the spinal fluid and exclusion of any underlying infectious cause. An MRI of the brain may be helpful in excluding such causes. The classical or acute form is characterized by the sudden onset of fever (103.6 is the mean but may be as high as 106), neck pain and stiffness and lethargy. 95% of dogs are younger than 2 years. Corticosteroids offer effective treatment, but relapse is common as treatment is tapered or withdrawn. The disease may be accompanied by immune-mediated polyarthritis and, at least in European studies, by kidney and heart involvement. C-reactive protein is elevated in dogs with SRMA and may be useful in monitoring the course of the disease but is not useful in predicting relapse.

The conference's keynote address was given by Anita Oberbauer, Ph.D., who is Professor of Animal Science and Associate Dean in the College of Agricultural and Environmental Sciences at the University of California, Davis. Dr. Oberbauer also received this year's AKC/CHF Asa Mays, DVM, Award for Excellence in Canine Health Research. Her discussion concerned the role of autoimmunity in the occurrence of those endocrine disorders marked by hypofunction and thus low production of essential hormones. (In contrast, endocrine disorders marked by hyperfunction with increased production of hormones are usually due to tumors.)

Hypothyroidism, hypoadrenocorticism and diabetes mellitus are among the most prevalent endocrine disorders in the dog and purportedly caused by an autoimmune attack of the endocrine tissue wherein the individual's immune system is dysregulated and mounts an attack against its own health tissues. Addison's Disease (hypo-adrenocorticoid production) occurs in 0.33% of all dogs and 0.38% of humans. Hypothyroidism occurs in 1.9% of all dogs, with a higher prevalence in the herding dog group. Type I Diabetes Mellitus occurs in 0.3-0.4% of all dogs. A genetic component seems to be involved in all these disorders, but the cause is not fully genetic. Unknown environmental factors, such as viral infections, also play a role. The strongest associations for many autoimmune diseases involve the histocompatibility complex (MHC) class II genes. In humans, many autoimmune diseases have common genes within the MHC complex. Genetic variations within the dog leukocyte antigen genes (DLA), the dog MHC

counterpart, have also been associated with autoimmune conditions. Three MHC class II genes are of importance in the dog and are designated DLA-DRB1, DLA-DQA1, and DLA-DQB1. Certain combinations, or haplotypes, in all three of these genes are associated with susceptibility to autoimmune disease of endocrine organs. Haplotype susceptibility signatures that are shared across breeds appear to combine with other genes to confer risk for specific endocrine disease as well as other common autoimmune conditions. Research in the field aims to identify genetic signatures to inform breeding decisions.

Linda Kidd, DVM, PhD, DACVIM (Small Animal Internal Medicine), Associate Professor of Small Animal Medicine at Western University of Health Sciences, College of Veterinary Medicine, discussed vector-borne infections which may initiate or mimic auto-immune disease. If the infecting organism has similar antigens to the host, autoimmunity may develop. Self-directed antigens may also be “unmasked” by the inflammatory response to infection. *Babesia* species infect red blood cells and can induce hemolytic anemia in experimentally infected dogs. Natural *anaplasma* infections may behave similarly. Immune-modulated thrombocytopenia has been described in tick-borne infections. Antiplatelet antibodies develop, and platelets may be sequestered in the spleen and blood vessels. Immune-mediated polyarthritis, with neutrophilic infiltration of joints may also occur in tick-borne infections. Although rheumatoid arthritis is rare in dogs, leishmaniasis may cause an erosive arthritis which is rheumatoid-factor positive. Protein-losing nephropathies have been documented in some cases of tick-borne infections due to the deposition of immune complexes in the kidneys.

Dr. Kidd recommended repeated PCR and serologic panels for the detection of tick-borne infections as antibodies to the infecting organisms may be absent in the acute blood samples.

Saturday afternoon’s session began with a presentation by Jason Stull, VMD, MPVM, PhD, DACVPM on the epidemiology of leptospirosis, caused by a gram-negative, spiral shaped bacterium. His data was derived from that of a commercial reference laboratory (Idexx Laboratories), and he tried to include some environmental data as well. Between 2009 and 2018 40,000 tests were performed for leptospirosis. 5% were positive. The greatest prevalence was in the upper Midwest, there were also 7 geographically distributed “space-time clusters” with 3-108 cases per cluster. Relative risk for young and old dogs was 1.4 -2.9. Males were at slightly greater risk. Similar data were obtained from Canada. Of 10,000 Canadian dogs tested, 8% were positive for leptospirosis by PCR testing.

Because of the high prevalence of positive tests in Chicago, a case-control study was then done in Chicago based on data from veterinary clinics located there. 45 cases were identified with 180 controls chosen from the same clinics as the cases, all dogs being seen during 2015-2018. Most dogs had been hospitalized. Case fatality rate was 29%. Relative risk for presence of the disease included young age (16 cases were younger than 6 months) with a relative risk of 2-4;

not neutered with a relative risk of 3; not vaccinated with a relative risk of 25. One case occurred in a fully immunized dog.

Regarding the advisability of immunization, Dr. Stull stated that it depended on the area. Standing water is a risk as is the exposure to racoons, skunks, rats and mice. (Chicago is believed to have an increased incidence because of its large population of rats.) Wild carriers typically do not show evidence of illness but shed the bacteria in their urine. Standing water, often contaminated with urine, is a risk factor. Dogs contract the disease through contacting contaminated water with mucous membranes or abraded skin. Organisms live for an extended period in the environment, especially wet environments, and urine-soaked bedding or urine-splashed water bowls and food present a risk to both other dogs as well as to their owners. Microscopic agglutination tests for IgG and IgM antibodies are traditional, but there are now rapid in-clinic PCR tests available. Immunization is given at 2 months of age, then 6 months later, and then yearly.

Edward B. Breitschwerdt, DVM, DACVIM (Small Animal Internal Medicine), Distinguished Professor of Medicine at North Carolina State University College of Veterinary Medicine, reported on his ongoing work with *Bartonella* species. These are highly fastidious, vector-borne, zoonotic bacteria that cause persistent intraerythrocytic bacteremia and endotheliotropic infection in reservoir and incidental hosts. The disease is transmitted by blood-sucking ticks and fleas. Several species have been associated with the development of vasoproliferative tumors in dogs and humans. The high prevalence of *Bartonella* species in dogs with hemangiosarcoma from North Carolina (74% of 109 dogs) suggests that the organism might have a role in the initiation or progression of this cancer. His current research will compare the prevalence of *Bartonella* DNA in tumor and blood samples from both splenic and cardiac hemangiosarcoma cases. He will also determine the prevalence of *Bartonella* in various geographical locations in the U.S.

Steven Dow, DVM, PhD, DACVIM (Small Animal Internal Medicine), faculty member at Colorado State University, Department of Clinic Sciences, gave an overview of cancer immunotherapy, currently utilized more in human than in animal medicine. Several types of immunotherapy exist. Non-specific activation of the immune system may generate anti-tumor activity. For example, tumor vaccines may elicit T cell responses but rarely produce effective tumor control. "Checkpoint" molecules regulate T cell function, and these are key targets for immunologic cancer therapy today. Monoclonal antibodies target inhibitory checkpoint molecules, of which there are at least 20, allowing exhausted T cells to reactivate and increase. The human patient response rate is about 20%. Two checkpoint antibodies are currently in development for canine cancer. PD-1 antibody is currently in development by Merck. PD-11 antibody, developed in Japan, is currently in Phase I trials. A third approach in immunotherapy is to alter

the immunosuppressive tumor microenvironment through the suppression of macrophages, which migrate to this area and induce immune suppression. Losartan, otherwise used to treat hypertension, has been found to block macrophage migration. Dr. Dow noted that hemangiosarcomas and osteosarcomas are the tumors most heavily infiltrated by monocytes (which develop into macrophages) in dogs. Palladia is another drug which significantly affects the tumor microenvironment and which is used in both human and dog cancers. Combinations of the different types of immunotherapy may prove to be very effective.

Erin Dickerson, PhD, Associate Professor at the College of Veterinary Medicine, University of Minnesota, discussed the role of propranolol, a beta-blocker typically used to treat heart disease, in human angiosarcoma where it has induced regression of the tumor and increased survival. It is a “cytostatic” agent, not cytotoxic and has been effectively combined with doxorubicin, a cytotoxic agent. A clinical trial for evaluation of this drug combination in the treatment of canine hemangiosarcoma, began July 1 at the University of Minnesota, funded by the AKC/CHF.

Jaime F. Modiano, VMD, PHD, Director of the Animal Cancer Care and Research Program of the College of Veterinary Medicine and Masonic Cancer Center of the University of Minnesota, spoke of the “Light at the End of the Tunnel,” with respect to the treatment of canine hemangiosarcoma. Dr. Modiano pointed out that hemangiosarcoma is not more prevalent in any specific breed of dog, occurring in all dogs, especially as they age. If there is a heritable component of risk, it is unknown. The most common mutations occurring in hemangiosarcoma are not specific for this disease. There is minimal overlap with those genes mutated in human angiosarcomas. Susceptibility probably derives from the wolf ancestors of dogs since wolves are also significantly affected by this cancer. The recent focus of Dr. Modiano’s work is to develop tests that provide a diagnosis early enough in the progress of disease, when treatment may be most effective, and pairing these tests with rationally designed therapy. Hemangiosarcoma is a drug and radiation resistant tumor which is believed to arise from cells related to bone marrow nurse cells that support formation of blood cells and blood vessels. Therefore, treatment very early in the development of these cells is necessary in order to kill them. Dr. Modiano’s team has developed “eBAT,” a new drug which he describes as an “epidermal growth factor bio-specific angio-toxin” and which eliminates sarcoma stem cells.

Sunday morning’s session began with a presentation by Brenda Bonnett, DVM, PhD, who is CEO of the International Partnership for Dogs. This is a non-profit international initiative to support quality, robust genetic testing. AKC as well as several European kennel clubs are members as is the Swedish national canine insurance company. One of the primary focuses of this organization is the development of a website for the “Harmonization of Genetic Testing for

Dogs,” which I have previously mentioned in my reports of the Delegate Canine Health Committee. The purpose of this website is to provide a database for genetic test providers (laboratories), who are encouraged to provide information on their quality measures. Currently the database provides information on more than 300 tests, from 30 major laboratories, for more than 400 dog breeds and breed-types. The website is: <http://www.dogwellnet.com> The IPPD plans to launch a proposed program to create comprehensive breed-specific packages that describe the health picture for breeds both nationally and internationally, including breed-specific recommendations for health testing.

Joshua A. Stern, DVM, PhD, DACVIM (Cardiology), Associate Professor of Cardiology, University of California, Davis, presented clinical and pathophysiology information on some common inherited cardiac diseases. Fortunately, none of these affect Australian Terriers.

In sub valvular aortic stenosis, the primary lesion is a sub valvular ridge or ring which obstructs outflow from the left ventricle and affects all components of left ventricular function. Most of the affected breeds have clear patterns of inheritance. In Bull Mastiffs, it is due to an autosomal recessive gene, most likely on Chromosome 21. In Golden Retrievers it is due to an autosomal recessive on Chromosome 13, and in Rottweilers, it is due to an autosomal recessive on Chromosome 38. In Newfoundlands, it is an autosomal dominant gene present on Chromosome 13 but not in the same location as the abnormal gene in Golden Retrievers. In this disease, cardiac beta-blocker drugs are effective treatment, extending life for about 4 years.

Pulmonic stenosis is also due to the presence of a ridge above or below the valve which prevents complete opening of the valve. This can be treated successfully in 95% of cases by percutaneous balloon valvuloplasty by which the valve is opened. The disorder appears to be due to an autosomal recessive gene in Chromosome 1, in both Bulldogs and French Bulldogs.

Atrial fibrillation is a common arrhythmia in both dogs and people. In Irish Wolfhounds it is due to an autosomal dominant gene. Novartis is currently working on a new drug to treat this condition in both dogs and humans.

Dilated cardiomyopathy is prevalent in Doberman Pinschers, and two gene mutations have been found to cause it, the “Titus Variant” being the more prominent. Of course, there have been recent warnings from the FDA of a potentially reversible, presumably non-genetic form of this condition occurring in many breeds. This has been associated with grain-free, boutique and exotic diets. University of California Davis has seen a significant increase in dilated cardiomyopathy, not apparently genetically related, in the past few years.

Dr. Jerome S. Bell, DVM, presented an outstanding presentation which updated and summarized much of what he had presented at our National Specialty at Asheville in 2018. I am

seeking permission from Dr. Bell to reprint this article in the *Talkabout* as it presents information critical to a successful approach to breed sustainability.

The final presentation of the conference, and in some ways the best, was by Leigh Anne Clark, PhD, Associate Professor Genetics and Biochemistry at Clemson University. Over a 12-year period of sustained research, she was able to work out the complex inheritance pattern of dermatomyositis, an autoimmune disease of the skin and muscle that primarily affects Collies and Shetland Sheepdog. Much of her work was supported by the Collie Club of America, working through the AKC/CHF. Dr. Clark was able to uncover genetic variations of the MHC (Chromosome 12), PAN2 (Chromosome 19), and MAP3K7CL (Chromosome 31) that are strongly associated with dermatomyositis. Of the 27 possible ways in which alleles at these 3 loci can be inherited, 9 combinations confer moderate to high risk for developing DMS and explain 93% of cases. The pattern of disease occurrence illustrates an interaction between genes as well as an inverse correlation between age of onset and the number of risk alleles. Environmental triggers and other minor loci also play a role in pathogenesis. The uniquely high frequencies with which these genes appear in Collies and Shetland Sheepdogs is, most likely, a consequence of breeding selection for desirable traits. In this case it is avoidance of the blue merle color, which is associated with deafness. Breeding strategies, therefore, cannot be focused on eliminating the highly frequent risk alleles, but rather on selecting breeding pairs that will produce puppies with low-risk genotypes. Thus, it would be impossible to breed away from the disease without the genetic tests developed by Dr. Clark over many years of dedicated work.

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