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Fall, 2007
It has been an exciting year for Wheaten health efforts…. The Canine Phenome Project at the University of Missouri is now able to accept and store blood samples from all Wheatens, and we are striving to collect a large number of samples to begin genetic research of our health problems; the PLE Project at TAMU has moved past the initial testing stage and now has monetary support of a drug company and they are looking for additional Wheatens affected with PLE or IBD to participate in the trial; the pANCA Project initiated by the Wheaten Health Initiative (WHI) with support from the SCWTC of Great Britain and a grant from The Kennel Club’s Charitable Fund has successfully completed five DNA Clinics; and we have celebrated the first year of publication of “Wheaten HealthNews”.

As we look to 2008, I encourage all Wheaten breeders and owners to take on the “Breeders Challenge” discussed in this issue. In the coming year, we will be setting up regional DNA Collection Clinics sponsored by local clubs, the SCWTC, the Endowment, and the GRF to support the Canine Phenome Project. The success of this project depends in large part on us, the Wheaten community. We need the participation of all breeders and owners…, this means donating DNA and also your dollars! We’ve set the goal; and now, with your help, we’ll reach it.

Best wishes for a wonderful holiday season and a happy, healthy 2008 for our two- and four-legged friends!!

For the love of the dogs,

– Cecily Skinner
The SCWTCA Endowment, Inc. announces the Breeders’ Challenge to benefit improved health among Soft Coated Wheaten Terriers. The health of our Wheatens is of paramount importance to us all. Health Research will be the key to a long and healthy life to our beloved show dogs and companions.

Our efforts are to target two worthy research projects: the Canine Phenome Project and the Siblings Pairs Study.

The goal of the Canine Phenome Project is to assemble a resource consisting of DNA samples from a wide variety of dogs with well characterized phenotypes and have it ready when the technology is ready. This will establish a DNA bank with supporting data for researchers to identify genes responsible for canine diseases and is now open to all Wheatens.

The Wheaten Siblings pairs study is to locate genes involved with PLE & PLN. Both projects are under the care of Dr. Gary Johnson at the University of Missouri, Columbia.

In an effort to shine light on these two significant research endeavors, the SCWTCA Board of Directors and the SCWTCA Endowment Board have endorsed a unique fund-raising program, The Breeders’ Challenge.

Who will take up the Challenge?

We invite and encourage all SCWTCA National club member breeders to contact the owners of Wheatens bred by them. We need as many as are able to contribute to this worthy cause. The SCWTCA Endowment, is a 501(c)3 nonprofit organization. Therefore, all donations are tax deductible. A decal of a running Wheaten will be sent to donors that contribute $25.00 or more to the Challenge.

The Endowment Board will provide a template/form letter that breeders can personalize. It will feature a “tear-off contribution sheet” that will include: the breeder’s name, a list of specific projects, including a general fund, and a list of available incentives. The template will be available to breeders as a Word attachment.

Donations can be submitted to the Endowment Treasurer as individual checks or in batches of checks. Donations will count towards the breeder’s total only if the breeder’s name and “Breeders’ Challenge” notation accompany the checks.

When should we begin?

Now! The Challenge will run until December 31, 2008. The winner will be the breeder whose owners donate the combined largest amount of money. Breeders’ own donations do not count towards the winning amount.

The first Breeders’ Challenge award winner will be notified in January 2009, and an award will be presented at the SCWTCA 2009 annual meeting. The first year’s award will be a head study painting of the breeder’s dog of choice created and donated by Darci Olson.

So get your Wheaten owners’ names and addresses ready! Set! Go!
IN DOGS, A SHORTCUT TO MAPPING DISEASE GENES

Nearly two years ago, Broad Institute researchers and their colleagues announced they had successfully decoded the genome of the domestic dog, a species coaxed into hundreds of distinct types through selective breeding by humans over the past two centuries. The research team also created a genome-wide catalog of about 2.5 million specific genetic differences – known as single-nucleotide polymorphisms, or SNPs – across various dog breeds. Now, an international team of researchers led by Broad scientists has applied those initial results to develop a tool for efficiently mapping disease genes in dogs. The tool, described in the September 30 advance online edition of Nature Genetics, may also help quicken the pace of efforts to understand the molecular basis of human diseases.

“Dogs are a unique species, domesticated and bred by humans who selected for traits like shape, size, color, and personality,” said Kerstin Lindblad-Toh, senior author of the new study, co-director of the Broad Institute’s Genome Sequencing and Analysis Program, and guest professor at the Department of Medical Biochemistry and Microbiology at Uppsala University in Sweden. “In addition to conserving desired traits, the selective breeding of dogs may make rare disease mutations common in a breed.”

While dogs and humans often share the same living spaces, they are also susceptible to many of the same illnesses, including cancer, epilepsy, and diabetes. And since the two species share much of their DNA, efforts to pinpoint the genetic underpinnings of dog diseases have the potential to deepen the knowledge of diseases in humans.

In dogs, it is well known that certain diseases tend to occur at higher rates within specific breeds. That is because, in the course of breeding, disease-associated genes have been inherited along with the genes for desirable traits. The recent sequencing of the dog genome revealed another consequence of selective breeding – a unique genome structure, characterized by chunks of DNA, called haplotypes, that are roughly 100 times larger than those found in the human genome.

This remarkable structure, with long stretches of DNA shared between dogs within one breed and shorter stretches common among dogs of different breeds, provides the researchers with a critical shortcut. The structure allows them to investigate canine diseases by using relatively few genetic markers and by analyzing fewer dogs. “Our new mapping methods take advantage of the power of reduced genetic diversity in dog breeds and the sharing of mutations across breeds to identify disease genes,” said Elinor Karlsson, first author of the new study and a graduate student in the Broad’s Genome Biology Program.

“We use a two-stage approach to first find the approximate neighborhood of the causative mutation, and then we zoom in on its specific location on the genome,” added Karlsson, who collaborated on the project with co-author Claire Wade, senior research scientist in the Center for Human Genetic Research at Massachusetts General Hospital and a Broad researcher.

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To aid their search for candidate disease genes in dogs, Karlsson, Wade, and Lindblad-Toh worked with Affymetrix to develop a microarray that recognizes approximately 27,000 of the 2.5 million identified SNPs in the dog genome. With support from the Broad’s Genetic Analysis Platform, the array enabled the researchers to identify the underlying genes for two traits: white coat color in boxers and the inverted ridge of hair growth in Rhodesian ridgebacks. In addition to showing a simple pattern of inheritance, suggesting that one gene or genomic region is responsible, the coat color and ridgeback traits are easily observed in dogs, making them ideal for testing the two-stage mapping strategy.

In the first stage of mapping the coat color trait, the researchers analyzed ten white and nine solid boxers using the microarray to pinpoint SNPs associated with white coat color. The highest-ranking SNP from their analysis resides in a section of the dog genome that contains one gene, called MITF, an important developmental gene associated with both pigment and auditory disorders in humans and mice. To more precisely characterize the color-controlling gene and identify the mutation(s) in white dogs, the study was expanded in the second stage to a larger sample of dogs, including both boxers and bull terriers, which also carry the white coat color trait. As a result, the team localized the causative mutation to an area of the dog genome that regulates the activity of the MITF gene.

Taking the same initial approach to map the hair ridge trait in Rhodesian ridgebacks, the scientists identified a segment of DNA that was found in all of the 12 ridged dogs, but in none of the 9 ridgebacks lacking a ridge. The region includes three fibroblast growth factor (FGF) genes that play crucial roles in development. Further analysis revealed the precise genetic cause of ridges in the dogs - the region containing the three FGF genes is abnormally duplicated, such that the three genes are present in excess copies.

A key advantage of trait mapping in dogs is that fewer individuals are needed for analysis compared to similar genome-wide studies in humans. After validating their approach on so-called Mendelian traits, which are controlled by a single gene or genomic region, Lindblad-Toh and her colleagues are now turning their attention to complex diseases. These diseases, such as cancers and autoimmune disease, involve multiple genetic and environmental causes. Importantly, many of the diseases are found not just in dogs, but in humans, too. Because of the unique genome of purebred dogs, the researchers may only need to test the DNA of a few hundred animals to characterize complex diseases, compared to the thousands of subjects that are required to study these diseases in humans.

An ongoing challenge in the effort is to collect blood samples from dogs of various breeds, including both healthy and sick animals. Since all blood samples used in this research come from pet dogs, both dogs and their owners are essential collaborators in continuing the research. At the website, www.dogDNA.org, the dog owner community can learn more about the types of samples that are most needed and how to participate.

**REFERENCES:**

Karlsson et al. (2007) *Efficient mapping of mendelian traits in dogs through genome-wide association.* Nature Genetics DOI:10.1038/ng.2007.10

Hillbertz et al. (2007) *Duplication of FGF3, FGF4, FGF19, and ORAOV1 causes hair ridge and predisposition to dermoid sinus in Ridgeback dogs.* Nature Genetics DOI: 10.1038/ng.2007.4

For more information, contact: Communications news@broad.mit.edu
SOFT COATED WHEATEN TERRIER DNA BANK

CANINE PHENOME PROJECT
ANIMAL MOLECULAR GENETICS LABORATORY
UNIVERSITY OF MISSOURI – COLLEGE OF VETERINARY MEDICINE

PURPOSE

The purpose of the Canine Phenome Project is to establish a DNA bank with supporting data for use by researchers to identify the genes responsible for canine diseases and other characteristics. For Wheaten owners, it is an opportunity to store DNA from Wheatens for future use by researchers interested in finding the genetic cause of PLE, PLN, RD and Addison’s or other diseases.

HOW IT WORKS

The Canine Phenome Project is a genetic research project. It receives blood samples, extracts the DNA and stores it for use in approved research. It also collects information about the individual dog contributing the DNA. Online survey forms are completed by the owner to record health and other information. The owner may update information at any time. Data on each individual dog is kept confidential unless the owner authorizes access.

HOW TO PARTICIPATE

1. Enroll your dog online at www.caninephenome.org

   · Click on “Enroll Your Dog”.
   · Click on “Sign Up Here”.
   · Enter your contact information including an email address. An individual password will be emailed to you immediately.
   · “Log-in” using the password sent to you.
   · Click on “Enroll a New Dog”.
   · Complete the “Identification” information for your dog (AKC number and name, call name, sex, date of birth, microchip or tattoo number, name and AKC number of sire and dam).
   · Click on “Submit DNA Sample” on dog’s profile page that appears next.
   · Print and sign the resulting “DNA Submission Form” to mail with the blood sample.

2. Follow the detailed instructions for collecting and shipping the sample listed on the “DNA Submission Form” (#1 above). Send the following to the address listed on that form:

   · Blood Sample
   · DNA Submission Form
   · Pedigree (if available)
   · Check for $20* payable to the University of Missouri

*The SCWTCA Endowment is paying half of the $40 fee for DNA processing (reducing the cost to owners to $20) for the first 1000 Wheatens’ blood samples sent.

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The Greater Denver SCWT Club staged its first blood collection clinic to support the Canine Phenome Project (CPP) at the University of Missouri. Owners from all over the United States attended the Greater Denver Specialty, and many brought their SCWTs for collection. Thirty-four dogs coming from Iowa, Nebraska, California, Arizona, Missouri, Indiana, and Colorado donated blood which was then sent to UofMO to be converted to DNA.

The process ran smoothly: Stan and Jinx Moore provided their motor home as a quiet place for the vet tech and her restrainer to work. While Jinx helped owners fill out paperwork, I was in the motor home completing forms and labeling test tubes. The dogs were wonderfully cooperative, so we were able to collect on all dogs in under two hours.

Due to the generosity of the SCWTCA, Inc., the SCWT Endowment, and the Genetic Research Fund (GRF), all cost of the clinic (including personnel expense, supplies and shipping expenses) were covered. Owners only paid the cost of the DNA processing at the UofMO. In addition, each owner received a commemorative Wheaten pin designed by Jerry Stack.

When we were finished, we felt a great sense of satisfaction that we were able to begin the necessary process of supplying DNA to the CPP. We have raised considerable funds and, as we continue to do so, we should be mindful that the money is raised to advance research. That research can only go forward with significant donations of DNA as well.

**PROCEDURE FOR ORGANIZING A DNA COLLECTION CLINIC**

1. Determine time and place of clinic. If clinic will be held outdoors, arrange for an enclosed space such as a pop-up tent with sides or a motor home.
2. Send mailer or mass email to interested owners to encourage participation and estimate number of dogs.
3. Instruct owners to enroll their dogs on the CPP website [www.caninephenome.org](http://www.caninephenome.org) before the clinic. Ask them to print out the “DNA Submission Form” and bring it to the clinic. Also ask them to bring a copy of their dog’s pedigree, if available.
4. Plan number of dogs to collect.
5. You can collect blood from approximately 15 dogs per hour. (This depends on your vet tech, of course.)
6. Provide enough supplies for about 15 more dogs than you expect. Some people at your event, may bring additional dogs.
7. Order “I Gave DNA” pins from Carol Carlson, kccarlson@comcast.net.

8. Send estimated budget to Elaine Azerolo, eazerolo@centurytel.net before the clinic. Up to $600 will be available to pay for the vet tech, veterinary supplies, and shipping.

HIRE A VET TECH OR VETERINARIAN TO PERFORM BLOOD COLLECTION

1. Some states will only allow veterinarians to make collections so be sure what is legal in your state.
2. Arrange for vet tech to bring all required supplies. Larger size collection tubes (6 cc. or larger) may need to be ordered in advance.
3. Be sure the vet tech you hire is one who regularly draws blood.
4. Vet tech should also provide the person who restrains the dogs. It should NOT be the dog’s owner.

SUPPLIES

1. EDTA (purple top) tubes to collect blood. For adult dogs, you will collect 5-10 cc. of blood; for young puppies, 3 cc. of blood (There are varying sizes of these purple top tubes. Make sure you have one that holds at least 6 cc. of blood.)
2. Needles (6 cc. syringes or larger)
3. Needle disposal
4. Sharpie markers to write on tubes
6. Pens to fill out forms
7. Table to place dogs on for collection (our tech preferred to do the collection with the dog on the floor, so ask ahead of time.)
8. Enclosed space if outdoors (e.g., pop-up tent with sides or motor home).
9. Small cooler with ice pack to store samples during clinic.
10. Buy a shipping container used for shipping fresh-chilled semen from your vet. If none are available, contact Toni Vincent, FecalAPIkit@aol.com. (Tell Toni that you do not need the Fecal API collection tubes). I was able to put 34 samples in one box.

COLLECTION AND SHIPPING

1. AFTER blood is drawn, label tube of blood with owner’s last name, call name of dog, and Phenome ID number from the DNA Submission Form that the owner downloaded from the website. If dog was not enrolled previously, have owner complete an “Individual Dog Information” form, assign it a number, and use this as the ID number.

It is very important to clearly label the tubes and mark with a sample number that corresponds to a sample number indicated on the registration form.

2. Put matching ID number on the paperwork. Also write how the $20 fee was paid (i.e., cash or check); if check, include the check number.
3. Give owner commemorative “I Gave DNA” pin.
4. Store samples in cooler during clinic. Then refrigerate samples immediately.
5. When all samples are collected, prepare for shipping. I taped tubes together so they would not bang around and break. If there are a large number of samples, bundle the tubes of consecutively numbered samples in plastic bags and list the numbers on the bag (i.e., Put tubes of samples #1-10 in one bag, #11-20 in another, etc.). Place tubes in center of shipping box. Then pad the tubes with newspaper.
6. Place frozen cold packs around newspaper.
7. Fold paperwork and insert in a Ziploc bag so no moisture gets to it. Place on top of packaging.
8. Call UPS or FedEx to determine last pickup time of the day. Pack and ship shortly before that time.
9. Deliver box to UPS or FedEx to ship overnight to University of Missouri.

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10. **Only** ship on Monday through Thursday. (No one will be available to receive packages over the weekend.)

11. If you collect on the weekend, store samples in the refrigerator until ready to send on Monday.

**Helpful Hints:**

1. Have vet tech in a quiet, private area to do the collection.

2. **Only** the tech, restrainer, and person marking tubes and paperwork should be present.

3. Another individual can organize the filling out of paperwork. That person can also keep the flow going: as one dog is finished, taking that dog and handing over the next dog with the paperwork.

4. If you are at an outdoor venue, you can use a pop-up tent and sides for privacy. I found some owners were anxious that their dogs would misbehave. It is easier on both the owner and the dog to be separated for this quick collection.

5. You will also need a cooler in which to keep the samples until the collection is finished. Then, samples will need to be taken for refrigeration.

6. You want the blood cold, *but not frozen*. Remember to put a buffer between the blood and the cold packs when shipping to avoid freezing.

7. Collection from any purebred Wheaten is accepted. While a pedigree is helpful, no dog will be turned away because it has come from rescue or a pet shop.

**Just For Fun:**

When it was time to collect from my puppy, I left. From outside, I could hear screaming (dog). Yes, mine won the award for the most difficult dog from whom to collect a blood sample. Go figure!

**UPDATE ON TAMU PROJECT**

- **Cecily Skinner**

Good news from Dr. Nora Berghoff, Texas A&M GI Lab, regarding the study they have undertaken with SCWTCA for dogs diagnosed with PLE (protein-losing enteropathy) or IBD (inflammatory bowel disease), but not PLN (protein-losing nephrology).

**From: Nora Berghoff: News About the Intestinal Permeability Study for SCWT.**

The company who supplies the trial drug in the study would like us to enroll another eight dogs. The data so far is not as clear, statistically, as desired; so a few more dogs are needed. Soooo, we will keep enrolling dogs for now.

But the good news is that the company has decided to start paying an incentive, amount unknown, for each Wheaten participating. They agreed to pay everyone, including those who have completed the study.

For specific information on how to participate, contact Dr. Nora Berghoff at [NBerghoff@cvm.tamu.edu](mailto:NBerghoff@cvm.tamu.edu).
The AKC Canine Health Foundation National Parent Club Canine Health Conference was held October 19-21, 2007 in St. Louis, Missouri. I attended representing SCWTCA; Jackie Gotlieb, SCWT Genetic Research Fund and Carol Carlson, SCWTCA Endowment, also attended. The conference was sponsored by the AKC/CHF and Nestle-Purina Pet Care. About 335 people attended, including representatives of 150 AKC Parent Breed Clubs.

The conference featured reports on the latest research in the canine health field. “Cytotherapeutics in Veterinary Medicine” was the keynote address presented by Rick Vulliet, DVM, PhD from the University of California - Davis. Cytotherapeutics is the therapeutic use of stem cells to repair damage from disease. Dr. Vulliet is working with adult canine bone marrow stem cells to treat degenerative myelopathy, a progressive neurological disease that causes hind quarter paralysis, and dilated cardiomyopathy that leads to congestive heart failure. Several breeds of dogs are affected, and there are human equivalent diseases. Use of stem cells is an emerging field of research with many unanswered questions, including effective treatment procedures and long term safety as well as ethical issues.

Dr. Vulliet was followed by Mark Oyama, DVM, DACVIM, University of Pennsylvania, who spoke on current diagnosis and treatment of cardiac disease including the potential use of stem cells. Cardiac disease is prevalent in many breeds. Diagnosis is expensive, and treatment is limited - usually just alleviating symptoms. For breeds weighing less than 40 pounds, mitral valve disease is the most common type of heart disease. There has been some progress in understanding inheritance of some types of cardiac disease.

Cancer research was another major topic at this year’s conference. Four speakers addressed canine cancer. Cancer is the most common disease cause of death. (This is true for Wheatens according to the 2000 SCWTCA health survey.) The incidence rate and type of cancer varies by breed. Life-time risk is estimated to be 30-50% for all dogs. Cancer is rare in young dogs. For companion dogs over the age of 10 years, 50% will die from cancer. Jaime Modiano, VMD, PhD, Comprehensive Cancer Center – University of Minnesota, said, “Life is the greatest risk factor”. Most cancers are treatable but, probably, are not preventable today.

Genetics, lifestyle, and environment may all play a role in cancer risk. Multiple genetic mutations are found in common canine cancers. The best documented lifestyle change to reduce cancer risk in dogs is to keep them lean and fit. Many commonly held beliefs about environmental effects on cancer risk have not been substantiated. Douglas Thamm, VMD, DACVIM, Colorado State University Animal Cancer Center, addressed some “myths” about canine cancer and its treatment. [Editor's Note: See Dr. Thamm’s article following this presentation summary.]

Rhonda Hovan used cancer in Golden Retrievers as an example of looking at disease from a breed club’s perspective. Hovan is an award-winning health and genetics writer and research facilitator for the Golden Retriever Club of America. She emphasized the importance of collecting good data on the incidence of a disease in a breed compared to other breeds, impact of the disease on lifespan and life quality, and, as in the case of cancer, specific types that are over-represented. Accurate reporting, routine use of necropsy with pathology, and a culture of openness among breeders are necessary to find answers. Jerold Bell, DVM, Tufts Cummings School of Veterinary Medicine, echoed Hovan’s emphases, recommending the use of an open registry database to compile information.
A basic genetics primer was presented by Anita Oberbauer, PhD, University of California – Davis, followed by comments on “Responsible Breeding Management of Genetic Disease” by Dr. Bell. He stated that health testing and knowledge of how to use test results is a requirement for responsible breeding. Related information from Dr. Bell may be found at [www.vin.com/tufts/2007](http://www.vin.com/tufts/2007). [See Dr. Bell’s article later in this issue.]

Heidi Parker, PhD, National Institutes of Health, described how the genetic classification of dog breeds into clusters as part of the genome project is making it easier to find genetic mutations for disease.

The complexity of genetic research was illustrated by a report on canine eye disease. Over 100 breeds are affected by Progressive Retinal Atrophy (PRA). Similarities end there since different gene mutations and modes of inheritance exist for PRA in different breeds. The promise of genetic research is for more rapid identification of genetic mutations, more DNA-based tests, and better therapeutic interventions including gene-therapy and more effective drugs, according to Simon Petersen-Jones, DVM, PhD, Michigan State University.

A genetic research success story was presented by Richard Goldstein, DVM, Cornell University. Dr. Goldstein was able to develop a test for the gene mutation associated with primary hyperparathyroidism in the Keeshond within a two-year period. This allows breeders to make informed breeding decisions and to identify at-risk dogs earlier.

Current infectious disease patterns were described by Christine Petersen, DVM, PhD, Iowa State University. Dr. Petersen stated that canine brucellosis is on the rise in some areas including Missouri and Iowa. It can devastate a breeding program, since there is no effective cure and it is difficult to remove from kennel premises. There is also a risk to humans.

Among new and emerging diseases are canine influenza and leishmaniasis. Influenza moved from horses to dogs in 2004. Leishmaniasis, found in 88 foreign countries, is now being brought to the United States by military personnel returning from the Middle East.

Other topics of interest to breeders and owners included spay/neuter benefit-vs-risk analysis, vaccines and vaccination schedules, nutrition for performance dogs, probiotics, nutrition for the immune system, degenerative cruciate rupture, and the Canine Health Information Center (CHIC). Updates on the AKC’s veterinary outreach program, public education program, and canine legislative activities were presented as well as an overview of CHF programs.

The 2007 AKC/CHF National Parent Club Canine Health Conference featured sixteen speakers from the scientific community, one from a parent breed club, three from the AKC, two from the CHF, one from CHIC, and three from Nestle-Purina Research Center. Posters from breed clubs and researchers were also on display during the conference. The two and one-half days were filled with information on the latest research and advances in canine health.
There is still a great stigma attached to a diagnosis of cancer, and it is natural for owners of dogs with cancer to equate cancer treatment in animals with experiences they may have had with treatment of themselves, their friends, or family members. Having an understanding of how cancer treatment in animals and humans differs can insure that dog owners make an informed decision when selecting treatment for their dog with cancer.

**Is cancer really a problem in dogs?**

Unfortunately, yes. It is the leading “natural” cause of death in dogs. Up to 50% of dogs will be affected by some type of tumor in their lifetime.

**Why does it seem like there is so much more cancer in dogs these days?**

Better health care = longer life. We are getting so good at managing other husbandry-related conditions in dogs (nutrition, infectious/parasitic disease, keeping pets indoors and on leashes) that they are now living long enough to develop more old-age conditions such as heart disease, kidney disease, endocrine disease, and cancer. Furthermore, now that there are more cancer specialists and options for treating cancer in pets, it is being reported more frequently.

**Did something in the environment play a role in my dog’s cancer?” Was I feeding the wrong food?**

There have been some associations proposed between certain types of cancer and environmental influences (canine lymphoma and certain herbicides or living in urban environments, canine mesothelioma and asbestos), but in the vast majority of cases, no such association can be made. Thus, based on what we know currently, food additives, lawn chemicals, pesticides, cosmic rays, etc. do not seem to significantly increase a dog’s risk of cancer.

**Why should I treat my dog with cancer?**

Because we can! We treat many animals with chronic disease that are never cured (diabetes, other endocrine diseases, heart disease), and cancer is another chronic disease. Furthermore, cancer is a disease that we can sometimes cure! Even in cases where cure is unlikely, there are many cancers where we can extend an excellent quality of life with treatment.

**Do we have to do XXX for this mass now? Can’t we just wait and see what happens?**

This applies to initial diagnostic tests (Let’s wait and see if it grows), additional surgery, or other treatments to prevent local re-growth after surgery (Let’s wait and see if it grows BACK), or therapy to delay or prevent spread (Let’s wait and see if it spreads).

- **Let’s wait and see if it will grow**: In general, delay in achieving a diagnosis only serves to increase the difficulty of treatment, and, potentially, the likelihood of spread. Larger tumor size is statistically associated with worse outcome for several important veterinary cancers, including canine mammary carcinoma and oral melanoma. The lump you are dealing with may very well be nothing, but if it is a tumor, the time to find that out is sooner rather than later.

- **Let’s wait and see if it grows BACK**: Locally recurrent tumors are statistically associated with a worse prognosis in certain diseases such as canine mast cell tumor and oral melano-
noma, and are suspected of being worse in others. For this reason, if a tumor is incompletely removed, the time to get aggressive is the very first time the tumor occurs.

• Let’s wait and see if it spreads: In general, treatment of gross metastatic disease is palliative at best. Asking drugs to kill a big bulky tumor is asking a lot, but asking those same drugs to have an effect against microscopic tumor cells in the lung or lymph node may be a much more reasonable goal. For example, the median survival time for dogs with osteosarcoma undergoing amputation, but not receiving chemotherapy until the time of metastasis, is approximately six months; whereas the survival time for dogs receiving chemotherapy for microscopic metastasis immediately after surgery is approximately 12 months.

**Doesn’t performing a fine needle aspirate/biopsy make the tumor “angry” and increase the risk of spread?**

NO. Getting from the primary tumor into the blood stream is only one of many hurdles a tumor cell must overcome to successfully spread. There are probably many circulating tumor cells in the body all the time, but it is only those few tumor cells with the complete genetic program that allow them to survive and grow at a distant site that will be able to successfully spread. Exceptions to this rule are:

1. Some mast cell tumors may become “inflamed” following a fine needle aspirate due to histamine release, although this in no way hastens spread. This is rarely serious and can be treated or prevented with an antihistamine such as Benadryl.
2. Needle aspiration/needle core biopsy of splenic and bladder masses is inadvisable, due to the risk of local tumor dissemination in the abdomen and/or seeding of the biopsy tract.
3. It is important that needle aspirates and biopsies of cutaneous/subcutaneous masses be planned so that the biopsy tract can be incorporated into the definitive surgical excision to prevent recurrence along the tract.

**Why don’t we just take the tumor off? Why do we need to do a fine needle aspirate/biopsy first?**

Obtaining a diagnosis prior to surgery helps to plan the surgical approach and lets the veterinarian know whether additional tests are indicated prior to surgery. This helps avoid situations like “Why didn’t you take X-rays before surgery?” and “Why should I have to pay for a second surgery if you ‘didn’t get it all’ the first time?” If surgical removal is used to obtain a diagnosis, it is important to understand that this is only being used as a diagnostic test, and that additional tests or treatments might be necessary, based on the results.

**Why should I pay for histopathology? Why don’t you just take it off and throw it away?**

If it’s worth removing, it’s worth submitting for microscopic evaluation. See “just wait and see” above for problems with the “we’ll submit it for histopathology if it recurs” approach. Similarly, it is important to avoid submission of parts of removed tissue or a “representative section” of a removed mass. This cuts the information gleaned from the pathology report in half, as surgical margins cannot be interpreted.

My Great Aunt Harriet had chemo, and she felt miserable all the time – I’d never do that to my dog! The drugs we use to treat cancer in animals are the same drugs that humans get, but we give considerably lower doses and don’t give as many at the same time to minimize the risk of adverse effects. With most chemotherapy protocols in common use, less than

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25% of patients experience unpleasant side effects, and 5% or fewer experience a severe side effect. The rare adverse effect necessitating hospitalization can usually be fixed in 24-72 hours. The likelihood of a chemotherapy-related fatality is less than 1 in 200. Should unpleasant side effect occur, doses can be reduced, drugs can be substituted, or additional medication dispensed to minimize the likelihood of further adverse effects. These changes are effective 90% of the time.

**OK, suppose my dog is the unfortunate one that has a side effect. What kind of things are we likely to see?**

This varies by agent, but in general the most common side effect is something related to the gastrointestinal tract – perhaps a few days of decreased appetite, mild nausea or vomiting, or loose stool. By the way of comparison, it’s usually not too different from what you might see if a dog got into the garbage. They might need to eat some bland food for a few days or take some anti-nausea or anti-diarrhea pills at home. Usually this doesn’t persist for more than 3-5 days. Some dogs have the potential to develop a low white blood cell (WBC) count. We check this quite frequently, and most of the time, it is not low enough to be dangerous. In some cases, a patient might need some oral antibiotics at home, or a treatment might need to be delayed for a few days. If a patient develops a serious side effect, it is usually either REALLY BAD vomiting/diarrhea (can’t keep anything down, getting weak/dehydrated) or dangerous lowering of their WBC count that renders them susceptible to a bacterial infection.

**I don’t want my dog to go bald!**

It is true that certain breeds (non-shedding breeds) can lose substantial amounts of hair from chemotherapy. It is rarely complete. Most other breeds experience little or no hair loss, although you may find more hair around the house, and long-haired breeds have the potential for excessive matting. Hair loss from chemotherapy is non-itchy and non-painful – it is a purely cosmetic change. Hair that is lost will typically begin to re-grow approximately one month following the completion of therapy.

**I don’t want my dog’s last weeks/months/years to be in and out of the hospital, like they were with Uncle Mac when he had cancer.**

Almost all veterinary chemotherapy treatments are done in an outpatient setting, and the majority involve quick injections rather than prolonged infusions (there are exceptions to this, however). Many protocols involve a series of treatments, followed by a period of careful observation. Continuous, indefinite chemotherapy is not the norm.

**But what about her age? Isn’t she too old for treatment?**

AGE IS NOT A DISEASE! Most of the patients we treat with cancer are older dogs. Statistics regarding effectiveness, survival, and tolerability of cancer therapy are usually generated in a population of older patients. Far more important than chronological age are general health (e.g., heart, liver, and kidneys) and how they are feeling.

**So what are our choices? We either do chemo or put him to sleep?**

Chemotherapy (and cancer therapy in general) is usually not an “all-or-nothing” proposition. For many tumor types, a spectrum of treatment options may be available depending on travel constraints, finances, risk of side effects, etc. For example, there are various treatments for canine lymphoma from which an owner can choose, including prednisone alone, prednisone plus doxorubicin, cyclophosphamide/vincistine/prednisone, or a multi-agent injectable proto-
col such as the UW-Madison protocol. All have different cost, risks of side effects, and numbers of trips required and varying degrees of effectiveness. For osteosarcoma, amputation and platinum-based chemotherapy may be the optimal treatment, but other options could include palliative radiation therapy or amputation plus doxorubicin.

**What about radiation therapy for my dog’s tumor?**

Radiation therapy can be very useful for certain tumors. Since it is a local treatment, it is **most often used to treat local disease**, e.g., tumors with a high likelihood of aggressive local infiltration and re-growth but a low risk of spread. Common examples include postoperative treatment of incompletely excised low-or intermediate-grade mast cell tumors, soft-tissue sarcomas, oral tumors such as fibrosarcoma, squamous cell carcinoma and dental tumors, and perianal tumors. It can be used prior to surgery in certain cases to render an inoperable tumor amenable to surgery. It can also be used to improve quality of life in some highly metastatic tumors such as osteosarcoma and malignant melanoma. The majority of “definitive” or “full-course” radiation therapy protocols in common use involve a series of 10-25 treatments delivered either Monday through Friday or three days per week for several weeks. Although there is no reason why these treatments cannot be delivered on an outpatient basis, many animals will spend some of the time in the hospital for practical, travel-related reasons. Most “palliative” or “coarsely fractionated” radiation therapy protocols will involve 1-6 weekly treatments on an outpatient basis.

**But won’t he be horribly sick from radiation?**

Radiation therapy is a **local** form of therapy - the radiation is only delivered to the site of the disease. Thus, systemic side effects (nausea, fatigue, bone marrow suppression) generally do not occur. However, **each treatment does require very brief anesthesia** or heavy sedation to insure that the radiation is delivered to the correct spot. In theory, there could be systemic adverse effects as a result of the anesthesia, but they are very rare in the patient with normal organ function.

**What about radiation burns?**

It’s true that animals receiving radiation therapy can develop varying degrees of sunburn-like reaction at the site where the radiation is delivered. These can range from mild redness and itchiness to moist, oozing, or ulcerated skin. Many animals will need to wear an Elizabethan collar to prevent self-trauma and/or receive oral antibiotics and/or pain medications during this period. These effects typically do not start until the second or third week of treatment and are resolved within 2-4 weeks after the completion of radiation therapy. The animal can be left with an area of irradiated skin that is permanently hairless; the hair may grow back only partially, and may turn white within the radiation field. Chronic, long-term side effects are rare with the exception in animals receiving radiation therapy for nasal, oral, or brain tumors.

**Will he be radioactive when he comes home?**

The standard form of radiation therapy in animals is **external beam**, i.e., radiation is shone down from an external source, practically not that different from a diagnostic X-ray except using higher energy particles. Animals undergoing radiation therapy pose no health risk to their owners and they are not radioactive.

(continued on next page)
**REFERENCES**


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**GENETIC TESTING AND COUNSELING: A TROJAN HORSE FOR DOG AND CAT BREEDS?**

-JEROLD S BELL, DVM, TUFTS CUMMINGS SCHOOL OF VETERINARY MEDICINE, N. GRAFTON, MA

[This article originally appeared in the proceedings of the 2007 Tufts’ Canine & Feline Breeding and Genetics Conference.]

Disease-causing genes are searched for by researchers, and the resulting genetic tests are desired by breeders. Once obtained, 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 abreeder 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.

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.

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We know that most individuals carry some unfavorable 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 eliminates 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.

**Historical Examples:**

At the onset of testing for the autosomal recessive gene for GM1-gangliosidosis in the Portuguese Water Dog, the carrier frequency was 16%. The breed in America originated from less than ten individuals imported in the late 1960s and early 1970s. The defective gene was brought into the breed by the ancestral Algarbiorum line, which was the dominant breeding line. Breeders recognized that the Alvalade line did not carry the defective gene for GM-1 gangliosidosis, and preferentially selected dogs from this line for breeding, making it the major influence in the breed. Unfortunately, the Alvalade line carried the gene for late-onset pcd-PRA, including several influential affected imports. This defective gene was not present in the Algarbiorum line. The end result of selection was the near elimination of one ancestral line, and a breed-wide carrier frequency of pcd-PRA of 35%.

In cat breeds, genetic testing for the autosomal dominant genes for polycystic kidney disease in Persian and Himalayan cats (38% affected worldwide) and hypertrophic cardiomyopathy in Maine Coon Cats (over 30% 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 over 30% of the breed would put a 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 amount of genetic bottlenecking could be devastating. Concurrently preserving the diversity of the gene pool over the next few generations while at the same time eliminating the defective gene is the most practical and desirable way to manage the disorders.
The American Burmese cat breed in recent years has split into a traditional and a contemporary head phenotype. Unfortunately, the contemporary phenotype that has been desired in the show ring is shown to be caused by the heterozygous genotype for the recessive, lethal, cranio-facial defect. Dr. Leslie Lyon’s laboratory at UC-Davis is in the process of identifying the defective gene. Once a genetic test is established, it will be seen how the breeders will utilize the test for the best interests of the breed.

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, knowledge of pedigree backgrounds, and relative risk pedigree analysis. 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.

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.

\[ S = \text{risk of being carrier from the Sire.} \]
\[ D = \text{risk of being carrier from the Dam} \]
\[ \text{Risk of being affected} = S \times D \]

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.

\[ \text{Carrier Risk} = S + D - (S \times D) \]

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

\[ \text{Carrier Risk} = \frac{S + D - (2 \times S \times D)}{1 - (S \times D)} \]

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.

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.

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 boney 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.

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.

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The AKC/CHF Parent Club Conference this October featured a Poster Contest with prizes offered in various categories. For the first time, the Soft Coated Wheaten Terrier Club of America submitted an entry. Roxanna Springer designed a wonderful poster featuring our club newsletter, "Wheaten Health News" and excerpts from the seminar “An Introduction to Genetics” presented by Dr. Neil O’Sullivan as well as information about the Colony Dogs project and the Health Tracker program.

This poster (reproduced on the following page) was awarded FIRST PLACE in the Canine Health Education & Communication category and SECOND PLACE in the Fund Raising category. Along
The first articles reported on the 2005 AKC CHF Health Conference, new and continuing canine health research efforts, and specific veterinary protocols for testing, diagnosis, and treatment. SCWT health research focuses primarily on protein-losing enteropathy and nephropathy (PLE/PLN), and juvenile renal dysplasia (JRD). Issues 2 & 3 featured SCWT health research in the UK, case studies of pyometra and Lyme disease, papers with researchers, and vaccination protocols. The Summer 2007 issue, included complementary (pANCA) research in the UK, details from a presentation in the UK by Dr. Meryl Littman (one of our researchers) on veterinary protocols, an aggression case study, and upcoming DNA collection and Health Seminar on Canine Cancers at MCKC 2007.

Professional geneticist and SCWTCA member, Nell O'Sullivan presented this genetics seminar held at a the GWTA working Specialty in June 2007. Sponsored by each of the SCWTCA's associated health programs, this seminar made genetics relevant for breeders.

Pages 11-12 provide a foundation of understanding of how genetics and breed development work together. Performance, conformation, temperament, appearance, and health standards require that breeders function as "working geneticists".

The genetic data combines with phenotypic and clinical information accumulated through the decades long Open Registry and Colony Dogs programs under the research direction of Dr. Meryl Littman and Dr. Shelly Varden, respectively. The Colony Dogs continue to provide information to enable effective early testing and treatment for SCWTs with PLE or PLN. Continuing the lifelong care of the Wheaten and Wheagles (SCWT/ Beagle mixes) is shared by SCWTCA members and pet owners through online listservs and fundraisers. The Informative Families and Geriatric Wheatens projects supplement the data with ongoing follow-up and with tissue samples according to online necropsy protocols. Because PLE and PLN do not evince themselves until SCWTs reach ages of 3-6 years or later, the hope is that trends of protein/creatinine ratios can identify affected dogs earlier to allow for earlier treatment and, therefore, longer and better quality of life for those SCWTs. The Health Tracker program was created by SCWTCA members for SCWT owners to be able to see trends in their dogs’ blood and urine testing throughout their lives. Because these trends often are not evident until after the dogs have already been championed and bred, finding the gene(s) involved in these problems is essential in limiting the diseases. One other benefit of the Health Tracker is the ease of sharing health information with researchers, veterinarians, and breeders. The Tracker is available online at the national club and the SCWTCA Endowment Fund websites.
with two beautiful Rosettes given to Roxanna, our club received $500.00 for First and $300.00 for Second that will be deposited in SCWTCA’s AKC/CHF Donor Advised Fund to be used for health research.

Many thanks go to Roxanna for her design, Leo Springer for printing and arranging to transport the poster, and Elaine Azerolo for presenting it at the conference. Roxanna and Leo also graciously donated all costs involved in making and shipping the poster.

We’re also happy to report that the Genetic Research Fund (GRF) won a FIRST PLACE in the Fund Raising category and will receive $500.00 in prize money for their Donor Advised Fund. Their terrific poster was designed by Judith Martin and presented at the conference by Jackie Gottlieb.

Everyone involved was thrilled to see two excellent entries for Soft Coated Wheaten Terriers and equally thrilled that both were winners!

**FOLLOW-UP TO THE GERIATRIC DOG AND INFORMATIVE FAMILY REPORT**

This is a follow-up to the Geriatric Dog and Informative Family Report published March through June 2007 in Wavelengths, the Health Newsletter, and Benchmarks, as well as posted on the scwtbreeder list. The latter three invited readers to submit questions for Dr. Littman to help us better understand her observations based on analysis of Penn DNA Bank samples from affected dogs (largest number of the samples), geriatric dogs, as well as dogs from the Informative Family and Wheagle Colony.

Only two individuals responded to the invitation. Their inquiries were combined with questions generated by SCWTCA’s liaisons to the Geriatric Dog, Informative Family and Open Registry projects. The questions and Dr. Littman’s responses appear below, but first a review of the key observations Dr. Littman offered in the Geriatric Dog and Informative Family Report:

- Apparently healthy geriatric dogs do not necessarily have normal phenotypes. Some of the dogs who appeared at 14 years or older to be asymptomatic, based on the absence of PLE or PLN clinical signs, were determined upon necropsy to exhibit early signs of one or both diseases.
- Because, upon necropsy, some of the apparently healthy geriatric dogs showed evidence of PLE and/or PLN, there does not appear to be an age cut-off for genetic expression of the diseases. Dr. Littman also suspected this since, on the Open Registry, there are dogs of advanced age affected with these diseases.
These observations illustrate the difficulty in determining the genetic make-up of a “normal” dog, i.e., one that will not exhibit changes on histopathology that are consistent with those seen in dogs affected with PLE or PLN upon necropsy.

It is anticipated that the Informative Family and Wheagle Colony dogs will produce a larger number of affected dogs than the normal population. As such, they are to be tested at least annually for clinical symptoms, with tissue samples submitted upon death for necropsy. When a genetic marker becomes available, this database will be invaluable.

**Questions arising from the above observations, and Dr. Littman’s responses follow:**

**Who analyzes tissue samples and makes the diagnosis, you or a pathologist?**

Usually a full time pathologist at The University of Pennsylvania or Dr. Brian Wilcock, Histovet Surgical Pathology, Guelph, ON Canada, has analyzed the necropsy tissue samples to help make the diagnosis in the past. Sometimes other veterinary pathologists have analyzed the tissue samples, and the reports were sent to Dr. Littman. The histopathology is only a piece of the puzzle to help make the diagnosis or characterize the cause of the dog’s illness. Other pieces of the puzzle include history, physical examination, blood and urine test results, etc. The diagnosis is a team effort made by interpreting all possible clues coming in from the owner, local veterinarian, clinical laboratory, and veterinary pathologist.

**There is a misconception that the pathologist sees only SCWT samples. Does the pathologist analyze samples from all breeds of dogs or SCWTs only?**

The pathologist analyzes samples from many purebred and mixed breed dogs.

**How is it determined based on tissue sample analysis following necropsy that an apparently healthy dog, one free of clinical symptoms while living, has PLN?**

Necropsy allows the pathologist to see the organ’s structure, and determine if there are changes. In the case of the kidney, the glomeruli are examined to determine the presence of changes consistent with PLN. Even if the glomeruli have not changed sufficiently to illicit symptoms or result in clinical signs, sometimes early structural changes can be detected. The changes seen by the pathologist are morphologic changes seen by examining the sample using ordinary light microscopy. But there could be functional changes that could lead to protein loss by the kidneys, that may not be seen by light microscopy. Currently we are not routinely doing extraordinary examinations of these kidney biopsies (for instance, electron microscopy or immunofluorescence, that could possibly show abnormalities of the glomeruli that would cause protein loss, but may not show up by ordinary light microscopy). Functional changes are best recognized by doing urine testing for protein, such as testing for microalbuminuria or doing a urine protein:creatinine ratio test.

Similarly, functional changes of PLE allowing for loss of protein from the intestine may not always be seen by light microscopy of the intestine. You can’t always tell how severe the protein loss is from looking at the morphologic changes under the microscope. That is why even mild inflammatory bowel disease (IBD) shouldn’t be ignored as a change, although pathologists may disagree about how mild, moderate, or severe IBD appears to them. Some pathologists may even interpret mild IBD as normal; but when we are dealing with a breed at risk, we have an added duty not to be too blasé about these findings, especially when trying to find the best “normals” for use in DNA studies. The functional changes of PLE are recognized by the blood test results (low albumin and globulin), and just as for PLN, the blood and urine test results are important pieces of the puzzle. In some geriatric cases, the blood and urine test

(continued on next page)
results were not done recently; and when all we have to look at is the histopathology changes, it makes it more difficult to know how severely the dog was affected. The experience of examining geriatric samples has taught us that it is best to try to get as many pieces of the puzzle as possible, including blood, urine, and histopathology, in order to make the best assessment of what exactly was going on in that individual at the time of death.

**What is the difference between a PLN affected kidney and one that has old age deterioration?**

The age-related changes of kidneys generally are not those of PLN, although an aged dog could conceivably show damage to the glomeruli that might mimic the changes seen in dogs with PLN, just as any breed of dog could show changes of inflammatory bowel disease (IBD), the changes seen in dogs with PLE. Diagnosis is made based on blood, urine, and histopathology criteria stated at the end of the OR. The criteria have not “evolved” - they are the same criteria we started with originally. In trying to tag a genetic DNA sample with a phenotype for purposes of the DNA bank, we define “normal” for geriatric dogs that do not have any changes in the kidneys or intestine that would be consistent with the changes that are seen in SCWTs with IBD, PLE, or PLN. Currently we are not listing geriatric dogs on the Open Registry based on mild histopathology changes alone, but neither are we tagging them as clear of these diseases and “normal” for the DNA bank.

![Abnormal glomerulus showing the changes typical of PLN.](image)

Kidneys, in my opinion, are the most likely organs to fail as any dog gets old. Kidney failure is very, very common - more common than heart failure or liver failure. However, the kidney failure seen in geriatrics is not usually caused by PLN. Common age-related kidney changes (that occur in any breed dog) are those that cause nephrons to drop out over time, so that the dog has decreased renal reserve, decreased ability to excrete toxic waste products of metabolism, and decreased ability to concentrate urine. Generally age-related kidney changes are not as protein-losing, nor do they cause hypoalbuminemia. The age-related changes typically show chronic interstitial nephritis changes on histopathology. The typical old dog’s kidney histopathology change shows more tubular changes and whole nephron dropout rather than predominantly glomerular changes. When glomerular disease causes renal failure, eventually
the tubules and whole nephrons are also affected. In a few cases of extreme “end-stage,” the kidney may be so scarred and fibrotic, that it can be difficult to know what the original cause of nephron damage and dropout was.

**What are the clinical or symptomatic (observable) differences between geriatric dogs with “old age” kidney changes versus geriatric dogs with PLN?**

Dogs with “old-age” kidney changes generally become thirsty and urinate a lot of dilute urine (polyuria/polydipsia with loss of ability to concentrate urine) as an early sign, even before they become azotemic with elevated BUN, creatinine, and phosphorus. They usually don’t have such high levels of protein in the urine that their serum albumin falls. In contrast, dogs with PLN may be able to concentrate their urine for longer than you’d expect, even after they become azotemic, and they may have proteinuria and hypoalbuminemia with possible thromboembolic events and/or hypertension even before they become azotemic or are in renal failure.

Eventually, as glomerular disease progresses, it does cause nephron dropout, polyuria/polydipsia; and, eventually, the changes on the biopsy might be so fibrotic and scarred and end-stage that it can be difficult to know what the initial cause was. When kidney function deteriorates a lot, the amount of protein in the urine might actually fall, because there are less nephrons able to filter the blood and less glomeruli to lose protein (and this is not necessarily a good sign).

**Among the geriatric dogs assumed to be apparently healthy or “normal” because they were asymptomatic while living, was it mild PLN, mild IBD or mild PLE that was detected upon necropsy?**

All three diseases were at times detected, and in a variety of combinations. Some samples revealed the presence of just one disease; others showed evidence of two diseases; and, in some in cases, all three diseases were apparent.

**When I count the number of samples discussed and subtract from the 228 total, it seems to yield a large number of samples without any category. (97+26=123 who are affected**
+ 24 others who are affected only upon histopathology + 33 normal without proper backup = 180.) Are all 48 remaining samples from “too young” or “pending” candidates? Can we get the full accounting of samples – for example, ‘some’ geriatric samples were tagged as having fetal glomeruli – is this number 2 or 3 or 10?

Yes, the remaining 48 samples include cases pending for histopathology results, samples sent in from dogs who died too young to make a full assessment of how to tag their DNA’s phenotype, and/or samples from dogs who are still alive but not old enough to make an assessment of how to tag their DNA’s phenotype yet (their health status is still being monitored).

The number of geriatric samples with fetal glomeruli was four. My pathologist tells me that there is disagreement among pathologists about how to interpret these; for instance, some would say they are “normal”, other pathologists would say they have mild changes of renal dysplasia, i.e., consistent with the changes seen in younger dogs with RD. In my opinion, if we want to be strict and as exact as possible for the genetic studies, these dogs shouldn’t be tagged as completely clear of doubt or considered “normal”.

How often should dogs who were used for breeding be tested and until what age?

We formerly recommended that dogs be tested until 7 years of age. It seems, now, that they should be tested throughout their lives. Following links from the SCWTCA website homepage (www.scwtca.org) to Health and, then, to Testing Protocols leads one to the:

- Annual Testing Protocols - Veterinarian Information
- Annual Testing Protocols - Owner Information

These resources suggest annual testing, and we have not deviated from that over the past few years. “Research suggests that any dog with UPC ratio in excess of 0.4 and no evidence of urinary tract infection should be closely monitored for the development of glomerular disease. This finding should be of particular concern in any breed of dog that is known to have familial glomerular diseases, such as the Wheatens.” Undoubtedly, testing more frequently than annual will be necessary to monitor the development of glomerular disease. Work with your vet to determine the appropriate interval based on previous test results, and ask your vet to consult Dr. Meryl Littman or Dr. Shelly Vaden for current recommendations and treatment. The contact information is available in Annual Testing Protocols – Veterinary Information.

How often should pets be tested?

To best protect the dog’s health, regardless of whether they were included in a breeding program, we recommend annual testing.

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**THE EFFECT OF HYPOTHYROID FUNCTION ON CANINE BEHAVIOR**

- L. P. Aronson*, W. J. Dodds

**PETLIFELINE**

**Editor’s Note:** Following our last issue that featured an article on Canine Aggression by Denise Lovelady, I was asked by a reader about the effect of thyroid on canine aggression. I contacted Dr. Jean Dodds, who is well known for her work with thyroid disease, and she very kindly sent the following articles.

**INTRODUCTION**

In human medicine, a wide range of behavioral symptoms have been reported in hypothyroid patients. In the early stages of the disease, reduced cognitive function and concentration, together with impaired short-term memory, may be easily confused with Attention Deficit-Hyperactivity Disorder (AD/HD) [Hauser et al 1993]. Visual and auditory hal-
lucinations can be mistaken for schizophrenia or psychosis. Fear – ranging from mild anxiety to frank paranoia; mood swings; and aggression have also been reported in hypothyroid patients [Denicoff et al 1990]. We have seen a similar range of behavioral problems in dogs (Canis familiaris), particularly in those whose hypothyroidism has not progressed to the more traditional skin, coat and metabolic changes characteristic of the condition.

Thyroid hormones modulate the activity of norepinephrine [Heal & Smith 1988], serotonin [Bauer et al 2002] and their receptors [Sandrini et al 1996]. In hypothyroid animals, 5-HT turnover increases in the brainstem, while cortical 5-HT concentrations and 5-HT2A receptor density may decrease. Administration of thyroid hormone to hypothyroid animals increases cortical 5-HT concentration and desensitizes autoinhibitory 5-HT1A receptors in the raphe area, thereby disinhibiting cortical and hippocampal 5-HT release. There is also evidence that thyroid hormones increase the sensitivity of 5-HT2 receptors [Bauer et al 2002].

In human medicine, thyroid hormones are frequently used to accelerate the anti-depressant effect of tricyclic antidepressants and selective serotonin reuptake inhibitors, which can often take 3 or 4 weeks to produce a noticeable psychiatric effect [Altshuler et al 2003; Sandrini et al 1996]. Gur et al [1999] demonstrated that in rats (Rattus norvegicus) administration of triiodothyronine (T3) for 7 days at a dose of 0.1 mg/kg SQ q 24h resulted in comparable elevation of basal 5-HT levels in the frontal cortex to those achieved after 4 weeks of clomipramine at a dose of 10mg/kg IPq24h. Thyroid hormones may also be given to supplement the effect of antidepressants when they are not achieving the desired effect.

Deficiencies of thyroid, adrenal cortex and sex hormones impair learning and the ability to store memories and behave normally. The adrenal hormones are directly involved in learning and behavior, while thyroid and sex hormones appear to modulate learning, memory and behavior at a higher level [Fedotova 2000]. Hypothyroidism often reduces cortisol clearance.

Conversely, glucocorticoids inhibit TSH release in response to thyrotropin releasing hormone [Otsuki et al 1973], reduce conversion of T4 to T3 [Chopra et al 1975] and have direct effects on the thyroid gland itself [Kemppainen et al 1983], so that stress could further diminish the function of a suboptimal thyroid. The thyroid-adrenal axis could be expected to affect behavior at all levels.

**Materials and Methods**

**Diagnosis**

Simply relying upon the total thyroxine (T4) test alone has been shown to give misleading results in an estimated 40% of dogs [Dodds 1997], whereas 62% of dogs were misdiagnosed with an in-house ELISA test kit [Lurye et al 2002]. Likewise, the canine thyroid stimulating hormone (cTSH) test produces false positive and negative results between 20-40% of the time, and so is considered to be only 70% predictive of primary canine hypothyroidism [Iversen et al 1999; Marca et al 2001]. Complete thyroid profiling (total and free T3 and total and free T4 levels, as well as circulating levels of thyroglobulin autoantibodies (TgAA), and T3 and T4 autoantibodies) should be performed. However, this information must be examined in conjunction with clinical evaluation of the animal. Reference ranges offered by most laboratories do not adequately address the disparate needs of different groups of dogs. Basal levels should be higher in toy and small breeds and somewhat lower in giant or very large breeds as well as sighthounds [Dodds 1995; Gaughan et al 2001; Hill et al 2001]. Basal levels should be higher in young dogs (up to about 18 months of age) and lower in geriatric animals [Wolford et al 1988; Dodds 1995].

A variety of circumstances can affect the optimal thyroid levels for an individual. These would include athletic/performance activities [Evason et al 2004]; altered levels of sex hormones – due to such causes as estrous, pregnancy or lactation; obesity; sickness or recent recovery from illness; vaccination; anesthesia or drugs that may influence thyroid function (continued on next page)
- corticosteroids, phenobarbital, potentiated sulfonamides, dietary soy or soy phytoestrogens, insulin, narcotic analgesics, salicylates, tricyclic antidepressants, furosemide, phenylbutazone and mitotane [Dodds, 1995 and 1997]. Superimposed upon these effects are daily diurnal fluctuations in hormone levels. It is possible to accurately assess thyroid function in the face of these conditions, but they cannot be ignored.

SUBJECTS

Thyroid function data were obtained for more than 1500 dogs presented to veterinarians for a range of behavioral problems. Some dogs were referred to the authors for treatment; others we consulted on but did not see personally. Thyroid function was determined based on laboratory results, clinical presentation, and other factors as described above. While some dogs would be deemed hypothyroid by any laboratory, others would be described as borderline or having suboptimal thyroid function. This is an ongoing study and earlier reports have been made on some of this data [Dodds 1997, 2004; Dodds & Aronson 1999, Aronson & Dodman 1997; Aronson 1998; Dodman et al 1995].

RESULTS

Of the 1500 cases presented for behavioral problems, 921 (61%) were determined to be hypothyroid or have suboptimal thyroid function using the determined criteria. Statistical analysis\(^1\) of the first 499 cases showed a highly statistically significant relationship between thyroid dysfunction and dog-to-human aggression (\(p=<0.001\), with a trend also towards dog-to-dog aggression (\(p\) slightly > 0.05). Other behaviors have not yet been statistically analyzed. Spayed and castrated animals are at greater risk than intact ones; mid sized and larger breeds are also more likely to be affected; the incidence is far greater in purebred dogs.

Treatment was initiated with levothyroxine sodium at a dose of 0.1mg/5.5–7.0 kg body weight, per os, q12h. (Doses were adjusted to allow for age, breed and other factors affecting the individual dog.) Follow-up was not available for all cases referred. In those for which it was available, 62% showed greater than 50% behavioral improvement, 36% showed more than 75% improvement to complete resolution of the problem, 25% showed between 25-50% improvement, 10% failed to improve, and 2% got worse. A favorable behavioral response to thyroid replacement therapy was usually apparent within the first week of treatment, although metabolic deficits were not corrected for three weeks, and skin and coat issues could take months to resolve.

BEHAVIORAL PRESENTATIONS

In dogs, as in humans, hypothyroidism presents as impaired mental function; reasoned behavior is lost in favor of a panicked response. In general, behavioral problems are most noticeable when the animal is psychologically or physiologically stressed.

The behaviors displayed by hypothyroid dogs fall into several distinct patterns.

In some animals problems appear at a very early age (6 months or less). They generally show poor or variable attachment to their owners, and they are difficult to train. Behaviors are lost from one training session to the next. Owners often describe these dogs as appearing to have AD/HD. These dogs may become fixated on one activity – such as playing Frisbee – and only value their owners’ presence for providing this.

Perhaps more common is the dog that exhibits a sudden change of personality and behavior at puberty or as a young adult. It may be that this is the age at which owners become more aware of the behaviors as the animal is larger and more difficult to live with, and odd behaviors that may be tolerated in a puppy become less endearing. Neutering usually has little or no effect on the behaviors, which may intensify as the dog ages. While certain breeds are over-represented, and distinct familial patterns may be observed, breed or lack thereof, cannot rule the condition out. Those breeds most represented include those in which

(continued on next page)
allergies and other immune problems are also most common. These would include: English Setter, Golden Retriever, Akita, Rottweiler, Doberman Pinscher, English Springer Spaniel, Shetland Sheepdog, and German Shepherd Dog. Like their younger cohorts, these dogs may show few, if any, signs of being hypothyroid other than behavioral ones. As opposed to being lethargic and obese, these dogs are often underweight and hyperactive. Many have a worried or tragic appearance. They may have seasonal allergies; recurrent skin, ear and foot infections; shed excessively; and/or chronic gastrointestinal problems. Some of these dogs present with a sudden onset of aggression - usually owner directed or intraspecies. Others will become fearful, whining incessantly, and showing nervousness in new situations or around strangers; they may hyperventilate and sweat excessively. Their fear may also lead to aggression. Some dogs develop obsessive behaviors such as tail chasing and pacing.

These same changes can occur in adult dogs. Separation anxiety may appear suddenly. Noise phobias – particularly thunderstorm phobia - most commonly arise in this group. This is also the stage at which some dogs start to show other signs of hypothyroidism – lethargy, weight gain, reduced energy, change in the character of the bark. Superstitious behaviors - watching the ceiling or wall for no apparent reason, refusing to walk on particular surfaces - may appear. Episodic dyscontrol and other behaviors related to partial seizures are also seen.

Although not a behavioral phenomenon per se, tonic clonic seizure activity is also commonly related to hypothyroidism. Particularly noticeable in performance and service dogs, some will lose concentration and no longer be able to perform at their previous skill level.

Older dogs may suddenly become irritable and show aggression, food guarding and other behaviors at complete odds to their younger selves. They sleep more, seek out heat sources, and show reduced scenting, hearing and visual acuity. While these signs might be attributed to advancing age or even cognitive dysfunction, they will resolve with treatment of the hypothyroidism along with the behavioral problems.

**Discussion**

The prevalence of hypothyroidism within the canine population is unknown, but is estimated in some breeds to be as high as 40 percent, and there is evidence that it is increasing [Dodds 1995]. A recent study [Hamilton Andrews et al 1998] compared total T4 and cTSH levels between a group of 21 Bearded Collies with no overt signs of hypothyroidism or aberrant behaviors (control group) with an experimental group of 22 Bearded Collies of similar age and sex distribution that exhibited problem behaviors but also showed no signs of hypothyroidism. Fifty-two dogs were excluded from the study because they exhibited signs of hypothyroidism, of these 34 had behavioral signs as well. Total T4 levels were significantly lower (p=0.01) in the experimental group when compared to the control group. The behaviors exhibited by the experimental group included noise and thunderstorm fears; fearful/anxious/shy behavior; separation anxiety; hyperactivity; poor concentration/learning; compulsive behaviors; mood swings, irritability and aggression – primarily territorial. We have seen more owner directed and dog-to-dog aggression, but otherwise behaviors seem similar to those we have found. Beaver and Haug [2003] also report owner directed aggression as a result of hypothyroidism.

We have seen a wide range of problem behaviors in dogs that are clinically hypothyroid or have suboptimal thyroid function. Some in this latter group appear completely healthy and others show minor problems such as seasonal allergy, ear infections, skin and coat disorders, etc. Many of these dogs responded to thyroid replacement on a twice daily dosing regimen. In some cases, the dogs have been treated with a variety of other psychoactive drugs prior to presentation, as well as a number of other medical regimens. In general, such treatment was unsuccessful.

While we know that thyroid can exert an effect on behavior by affecting levels of sero-
tonin and norepinephrin, it would seem there are other mechanisms involved in producing some of its behavioral effect. Given that levels of endogenous glucocorticoids inhibit thyroid hormone production and release, as well as the conversion to the active form, it is not surprising that in dogs with borderline and sub-optimal thyroid function, stress will induce a truly hypothyroid state that manifests initially in behavioral problems.

Our results suggest that thyroid replacement has an important role in the treatment of canine behavior, just as it does in human psychiatry. Therapeutic doses of levothyroxine are not harmful, provided any withdrawal of treatment is made gradually; wider use of such therapy could be beneficial to many dogs. In our opinion, it would be prudent to include a full thyroid panel in the work-up of most, if not all, behavioral cases.

1 The authors wish to thank Dr. Robert Keller, Chair, Computer Sciences, Harvey Mudd College, Pomona, CA for his statistical analysis of the data.

References


Aronson LP and Dodman NH 1997 Thyroid function as a cause of aggression in dogs and cats. Proceedings Deutscher Veterinärmedizinischen Gesellschaft p 228


Chopra I J, Williams DE, Orgiazzi J and Solomon DH 1975 Opposite effects of dexamethasone on serum concentrations of 3,3',5 triiodothyronine (T3). Journal of Clinical Endocrinology & Metabolism 41:911-920


Dodds WJ 1997 What’s new in thyroid disease? Proceedings American Holistic Veterinary Medical Association pp 82-95


Dodds WJ and Aronson LP 1999 Behavioral changes associated with thyroid dysfunction in dogs. Proceedings American Holistic Veterinary Medical Association pp 80-82

Dodman NH, Mertens PA and Aronson LP 1995 Aggression in two hypothyroid dogs. Journal of the American Veterinary Medical Association 207:1168-1171

Evasion MD, Carr AP, Taylor SM and Waldner CL 2004 Alterations in thyroid hormone concentrations before and after athletic conditioning. American Journal of Veterinary Research 65: 333-337

Fedotovn YO 2000 The effects of peripheral endocrine hormone deficiencies on the processes of behavior, learning and memory. Neuroscience and Behavioral Physiology 30:373-378


Heal DJ and Smith SL 1988 The effects of acute and repeated administration of T3 to mice on 5-HT1 and 5-HT2 function in the brain and its influence on the actions of repeated electroconvulsive shock. Neuropharmacology 27:1239-1248


Iversen L, Jensen AL, Hoier R and Aaes H 1999 Biological variation of canine serum thyrotropin (TSH) concentration. Veterinary Clinical Pathology 28:16-19


(continued on next page)
Hypothyroidism is the most common endocrine disorder of dogs, and up to 80% of cases result from an autoimmune disease that progressively destroys the thyroid gland (autoimmune thyroiditis). Once more than 75% of the gland is destroyed by this process, classical clinical signs of hypothyroidism appear. Because the condition is heritable, it has significant genetic implications for breeding stock. Accurate diagnosis of the early stages of autoimmune thyroiditis offers important genetic and clinical options for prompt intervention and case management. However, it is often difficult to make a definitive diagnosis.

As the thyroid gland regulates metabolism of all body cellular functions, reduced thyroid function can produce a wide range of clinical signs (see Table 1 on next page). Many of these clinical symptoms mimic those resulting from other causes and so recognition of the condition and interpretation of results of thyroid function tests can be problematic.

**Baselihg Thyroid Profiles**

A complete baseline thyroid profile is measured and typically includes total T4, total T3, free T4, free T3, T3 autoantibody (T3AA), and T4 autoantibody (T4AA), and can include canine endogenous thyroid stimulating hormone (cTSH) and/or thyroglobulin autoantibody (TgAA) (see Table 2 on p.31). The TgAA assay is especially important in screening breeding stock for heritable autoimmune thyroid disease. Affected dogs should not be used for breeding.

The normal reference ranges for thyroid parameters of healthy adult animals tend to be similar for most dog breeds, with exception of the sight hounds and giant breeds of dogs which have lower basal levels. Similarly, because young animals are still growing and adolescents are maturing, optimal thyroid levels are expected to be in the upper half of the references ranges. For geriatric animals, basal metabolism is usually slowing down, and so optimal thyroid levels are likely to be closer to midrange or even slightly lower.

**Genetic Screening for Thyroid Disease**

Thyroid testing for genetic screening purposes is less likely to be meaningful before puberty. Screening is initiated, therefore, once healthy dogs and bitches have reached sexual maturity (between 10-14 months in males and during the first anestrous period for females following their maiden heat). As the female sexual cycle is quiescent during anestrous, any influence of sex hormones on baseline thyroid function will be minimized. This period generally begins 12 weeks from the onset of the previous heat and lasts one month or longer. The interpretation of results from baseline thyroid profiles in intact females will be more reliable when they are tested in anestrous. Once the initial thyroid profile is obtained, dogs and
bitches should be rechecked on an annual basis to assess their thyroid function and overall health. Generation of annual test results provides comparisons that permit early recognition of developing thyroid dysfunction. This allows for early treatment, where indicated, to avoid the appearance or advancement of clinical signs associated with hypothyroidism.

(continued on next page)
Most confirmed cases of thyroiditis have elevated serum TgAA levels, whereas only about 20-40% of cases have elevated circulating T3 and/or T4AA. False negative TgAA results also can occur in about 8% of dogs verified to have high T3AA and/or T4AA. Furthermore, false positive TgAA results may be obtained if the dog has been vaccinated, especially with rabies vaccine, within the previous 30-45 days, or in some cases of non-thyroidal illness.

Canine autoimmune thyroid disease is very similar to Hashimoto’s thyroiditis of humans, which has been shown to be associated with the tissue major histocompatibility complex (MHC) genes. A similar association with MHC genes in hypothyroid dogs has recently been reported in Doberman Pinschers, English Setters and Rhodesian Ridgebacks. The presence of this unique genetic determinant doubles the risk of a dog developing hypothyroidism. This exciting finding hopefully will lead to development of a genetic marker test to identify affected breeding stock so that the disease incidence in pure-bred dogs can be reduced.

**Polyglandular Autoimmunity**

Individuals genetically susceptible to autoimmune thyroid disease may also become more susceptible to immune-mediated diseases affecting other tissues and organs, especially the bone marrow, liver, adrenal gland, pancreas, skin, kidney, joints, bowel, and central nervous system. The resulting “polyglandular autoimmune syndrome” tends to run in families and is believed to have an inherited basis.

<table>
<thead>
<tr>
<th>TABLE 2. Diagnosis of Thyroid Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>C Complete Basic Profile</strong></td>
</tr>
<tr>
<td>• (T4, T3, FT4, FT3, T4AA, T3AA)</td>
</tr>
<tr>
<td><strong>C Additional Tests</strong></td>
</tr>
<tr>
<td>• (TSH, TgAA)</td>
</tr>
<tr>
<td><strong>C Older Tests (T4, T4 + T3)</strong></td>
</tr>
<tr>
<td>Serum T4 and/or T3 alone are not reliable for diagnosis because:</td>
</tr>
<tr>
<td>• overdiagnose hypothyroidism</td>
</tr>
<tr>
<td>• underdiagnose hyperthyroidism</td>
</tr>
<tr>
<td>• fail to detect early compensatory disease and thyroiditis</td>
</tr>
<tr>
<td>• influenced by nonthyroidal illness</td>
</tr>
<tr>
<td><strong>C Newer Tests</strong></td>
</tr>
<tr>
<td>Free (Unbound) T4</td>
</tr>
<tr>
<td>Less likely to be influenced by nonthyroidal illness or drugs</td>
</tr>
<tr>
<td>Valid</td>
</tr>
<tr>
<td>-- equilibrium dialysis</td>
</tr>
<tr>
<td>• solid–phase analog RIA</td>
</tr>
<tr>
<td>• chemiluminescence solid–phase</td>
</tr>
<tr>
<td>Less reliable; liquid–phase analog RIA</td>
</tr>
<tr>
<td>Endogenous Canine TSH</td>
</tr>
<tr>
<td>In primary hypothyroidism, as free T4 levels fall, pituitary output of TSH rises</td>
</tr>
<tr>
<td>-- equilibrium dialysis</td>
</tr>
<tr>
<td>• elevated TSH usually indicates primary thyroid disease</td>
</tr>
<tr>
<td>• 20–40% discordancy observed between expected and actual findings</td>
</tr>
<tr>
<td>• published normal ranges may need revising upwards</td>
</tr>
<tr>
<td>• affected by concomitant chronic renal disease</td>
</tr>
<tr>
<td>Canine TgAA</td>
</tr>
<tr>
<td>Thyroglobulin autoantibodies are present in serum of cases with lymphocytic thyroiditis.</td>
</tr>
<tr>
<td>• positive results confirm diagnosis; 8% false negative</td>
</tr>
<tr>
<td>• 20–40% of cases have circulating T3 and/or T4AA</td>
</tr>
<tr>
<td>• allows for early diagnosis and genetic counseling</td>
</tr>
</tbody>
</table>

(continued on next page)
ABERRANT BEHAVIOR AND THYROID DYSFUNCTION

The principal reason for pet euthanasia stems not from disease, but undesirable behavior. While this abnormal behavior can have a variety of medical and psychological causes in animals, it recently has been associated with thyroiditis and hypothyroidism in dogs, and hyperthyroidism in cats. Typical clinical signs include unprovoked aggression towards other animals and/or people, sudden onset of seizure disorder in adulthood, disorientation, moodiness, erratic temperament, periods of hyperactivity, hypoattentiveness, depression, fearfulness and phobias, anxiety, submissiveness, passivity, compulsiveness, and irritability. After episodes, most of the animals appeared to come out of a trance like state, and were unaware of their bizarre behavior.

The typical history starts out with a quite, well-mannered and sweet-natured puppy or young adult dog. The animal was outgoing, attended training classes for obedience, working, or dog show events, and came from a reputable breeder whose kennel has had no prior history of producing animals with behavioral problems. At the onset of puberty or thereafter, however, sudden changes in personality are observed. Typical signs can be incessant whining, nervousness, schizoid behavior, fear in the presence of strangers, hyperventilating and undue sweating, disorientation, and failure to be attentive. These changes can progress to sudden unprovoked aggressiveness in unfamiliar situations with other animals, people and especially with children.

Another group of dogs show seizure or seizure-like disorders of sudden onset that can occur at any time from puberty to mid-life. These dogs appear perfectly healthy outwardly, have normal hair coats and energy, but suddenly seizure for no apparent reason. The seizures are often spaced several weeks to months apart, may coincide with the full moon, and can appear in brief clusters. In some cases the animals become aggressive and attack those around them shortly before or after having one of the seizures.

In dogs with aberrant aggression, a large collaborative study between our group and Dr. Dodman and colleagues at Tufts University School of Veterinary Medicine has shown a favorable response to thyroid replacement therapy within the first week of treatment, whereas it took about three weeks to correct their metabolic deficit. Dramatic reversal of behavior with resumption of previous problems has occurred in some cases if only a single dose is missed. A similar pattern of aggression responsive to thyroid replacement has been reported in a horse.

Of the initial 634 canine cases of aberrant behavior, 90% (568 dogs) were purebreds and 10% were mixed breeds. There was no sex predilection found in this case cohort, whether or not the animals were intact or neutered. Sixty-three percent of the dogs had thyroid dysfunction as judged by finding three or more abnormal results on the comprehensive thyroid profile. The major categories of aberrant behavior were aggression (40% of cases), seizures (30%), fearfulness (9%), and hyperactivity (7%); some dogs exhibited more than one of these behaviors. Within these four categories, thyroid dysfunction was found in 62% of the aggressive dogs, 77% of seizuring dogs, 47% of fearful dogs, and 31% of hyperactive dogs.

Outcomes of treatment intervention with standard twice daily doses of thyroid replacement were evaluated in 95 cases, and showed a significant behavioral improvement in 61% of the dogs. Of these, 58 dogs had greater than 50% improvement in their behavior as judged by a predefined 6-point subjective scale (34 were improved >75%), and another 23 dogs had >25 but <50% improvement. Only 10 dogs experienced no appreciable change, and 2 dogs had a worsening of their behavior. When compared to 20 cases of dominance aggression treated with conventional behavior or other habit modification over the same time period, only 11 dogs improved more than 25%, and of the remaining 9 cases, 3 failed to improve, and 3 were euthanized or placed in another home. These initial results are so promising that complete thyroid (continued on next page)
diagnostic profiling and treatment with thyroid supplement, where indicated, is warranted for all cases presenting with aberrant behavior.

Our ongoing study now includes over 1500 cases of dogs presented to veterinary clinics for aberrant behavior. The first 499 cases have been analyzed independently by a neural network correlative statistical program. Results showed a significant relationship between thyroid dysfunction and seizure disorder, and thyroid dysfunction and dog-to-human aggression.

Collectively, these findings confirm the importance of including a complete thyroid antibody profile as part of the laboratory and clinical work up of any behavioral case.

REFERENCES


CANINE BEHAVIORAL ASSESSMENT

As a follow-up to the article in our last issue regarding Canine Aggression, we’d like to let our readers know about a great, online behavioral questionnaire that is available. I took the survey, and it only takes a short time to complete; and when you are finished, you will receive an assessment of your dog based on your answers. There are also some excellent links included as well as where to go if you feel you would like professional help with your dog’s behavior. I hope this will be a good start to resolving any behavior issues your dog is experiencing.
Here is the updated news on the pANCA Research Project in Soft-Coated Wheaten Terriers, in the UK.

Briefly, for anyone who does not know the background, this project is the culmination of two years of work, which began with a seminar, organised by Wheaten Health Initiative (an independent UK health group for all owners and breeders of Wheatens). One of our speakers was Dr. Karin Allenspach, Dr.Med.Vet. FVH Dipl ECVIM-CA MRCVS, Lecturer in Small Animal Medicine at the Royal Veterinary College, who had previously worked with Dr. Shelly Vaden’s team with the NCSU Colony Dogs.

Dr. Allenspach indicated, during her presentation, that she was interested in further exploring the use of the test for pANCA (perinuclear, anti-neutrophilic, cytoplasmic antibodies – used for identifying Crohn’s disease in humans) with a wider Wheaten population as she believed it may be useful in identifying dogs at risk of developing protein-losing diseases.

In February of this year, Dr. Allenspach was given the go-ahead for the study by the RVC, and the work began for Wheaten Health Initiative. The original target required 200 blood samples from Wheatens; preferably 100 were to be from the 2-4 year age range and 100 from Wheatens over 4 years of age. This was always going to be a tall order, particularly in the younger age groups, but we were determined to do all that we could to make it possible.

The first step was to approach the Committee of the SCWT Club of Great Britain and ask for their help in spreading the word about the project. We also successfully applied for a small grant from the Kennel Club’s Charitable Fund to help with the costs of arranging sampling sessions, as we are an independent group relying solely on our own fund-raising efforts and the goodwill of our supporters.

We have organised five testing sessions in a variety of locations around the country, one of which was hosted by the SCWT Club of GB prior to one of its regular “Fun Days”. The last session was held on Sunday, November 11th (rather fittingly, it was also Remembrance Day). We have achieved a total of 186 Wheaten blood samples, exceeding our target with the older age groups but with slightly less than hoped for in the younger ones.

However, Dr. Allenspach is confident that she has sufficient data to complete her work and, together with Dr. Barbara Wieland, Med.Vet. PhD, Lecturer in Veterinary Epidemiology and Co-course Director MSc Control of Infectious Diseases in Animals at the RVC, will produce a scientific report of the findings in due course. Dr. Allenspach will also be re-testing some of those in the younger age groups and following up a random sample of dogs longitudinally over the next 2-3 years. She hopes that all those who have taken part in the project will continue to monitor and to inform her of any changes in their dogs’ health throughout their lifetime.

We could not possibly have achieved this without the goodwill and support of so many people. Particularly notable was the number of owners of companion Wheatens, who came along to testing sessions simply for the love of their dog and were also able to find out about the kind of information and help that Wheaten Health Initiative provides.

A number of breeders also gave their support, not only by bringing their own dogs but also by encouraging their puppy owners. However, it also has to be said that some of those in this country who have bred substantial numbers of puppies, sometimes over many years, were disappoint-
ingly absent from the testing sessions, despite all attempts to encourage their participation.

On a happier note, there was a breeder whose car broke down, with the dogs onboard, on the day of testing. Another breeder volunteered to drive a total of about 350 miles to collect the four Wheatens, bring them to the session and then deliver them back to their owner. What an amazing example of love for the breed!

You can visit our website: www.wheatenhealthinitiative.com for further information on the progress of this research, where you will also find a list of those who have participated and agreed to be recognised publicly, in order to demonstrate their support of the project.
NEWS FROM OFA REGARDING VPI REQUIREMENT AND FEE INCREASE FOR 2008

For more information on what constitutes an accepted verification of permanent identification (the PI assignation within the OFA number), see www.offa.org/vpi.html.

VPI FAQ

Beginning in 2008, verification of permanent identification must be performed in order for the data to be forwarded to the AKC for inclusion in their records. Dogs with the verification step completed will have a suffix of VPI assigned to their OFA numbers. Veterinarians are encouraged to make the verification part of their standard procedure for taking OFA hip and/or elbow films, and there is now an area on the OFA form for the veterinarian to indicate whether or not they verified the supplied permanent identification. Owners are encouraged to brief their vets on this policy change and when necessary proactively request that the verification step be performed.

Why is a DNA profile an unacceptable form of VPI?

While DNA profiles are able to uniquely identify individual dogs, it is the AKC’s policy to limit permanent identification for health screening purposes to tattoo or microchip. The rationale is that DNA profiles are not immediately verifiable. They require a sample to be taken and subsequent laboratory analysis. The AKC’s premise is that tattoos are visually immediately verifiable, microchips are immediately verifiable using a scanner, and that the verification should be done by the veterinarian at the time of testing.

What if I have an older Hip and Elbow application form, a different form, or want to get an already tested dog’s NOPI status changed to PI status?

There is a special VPI Application form on the OFA website that you and your veterinarian can fill out to attach to an older form, a form that currently doesn’t have the VPI info on it, or to change your dog’s status. It can be found at www.offa.org/vpiapp_bw.pdf.

OFA Fee Increase

For the first time since 2001, the OFA will be increasing its fees on some of its tests. The OFA now accepts credit cards for all application payments, and there is a space at the bottom of each application for that information.

Starting January 1, 2008, fees will increase for the OFA Hip and OFA Elbow databases. The table below shows the current fees along with the new fees.

<table>
<thead>
<tr>
<th>Applications Received:</th>
<th>before 12/31/07</th>
<th>after 1/1/08</th>
</tr>
</thead>
<tbody>
<tr>
<td>Animals Over 24 Months</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hip dysplasia database only</td>
<td>$30.00</td>
<td>$35.00</td>
</tr>
<tr>
<td>Hips plus elbows (together)</td>
<td>$35.00</td>
<td>$40.00</td>
</tr>
<tr>
<td>Elbow dysplasia database only</td>
<td>$25.00</td>
<td>$35.00</td>
</tr>
<tr>
<td>Litter of 3 or more submitted together</td>
<td>$75.00</td>
<td>$90.00</td>
</tr>
<tr>
<td>Kennel Rate—Individuals submitted as a group, owned/co-owned by same person</td>
<td>$15 per study</td>
<td>$15 per study</td>
</tr>
<tr>
<td>Minimum of 5 individuals</td>
<td>$15 per study</td>
<td>$15 per study</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Animals Under 24 Months</th>
<th>before 12/31/07</th>
<th>after 1/1/08</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preliminary hip evaluation</td>
<td>$25.00</td>
<td>$30.00</td>
</tr>
<tr>
<td>Preliminary elbow evaluation</td>
<td>$25.00</td>
<td>$30.00</td>
</tr>
<tr>
<td>Preliminary hips plus elbows (together)</td>
<td>$35.00</td>
<td>$40.00</td>
</tr>
<tr>
<td>Litter of 3 or more submitted together</td>
<td>$45.00</td>
<td>$60.00</td>
</tr>
<tr>
<td>Consultation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other radiographic studies</td>
<td>$25.00</td>
<td>$30.00</td>
</tr>
</tbody>
</table>

For now, fees on all other OFA tests remain unchanged.
HOLIDAY GIFTS FOR THE COLONY DOGS

If you would like to send a Holiday gift to the Colony Dogs at North Carolina State University, they would be thrilled to receive the following items:

- Shampoo and conditioner
- Large nail clippers
- Large UNFLAVORED Nylabones
- Gift cards to any online pet supply store (Petco, PetSmart, PetEdge, etc.)
- #7 Clipper Blades for Oster brand clippers

Please send your gifts to:

Tonya Harris  
North Carolina State University  
College of Veterinary Medicine  
4700 Hillsborough Street  
Raleigh, NC 27606

FOR PAYPAL: If anyone wants to use PayPal to send money to buy a holiday gift for the Colony Dogs, please go to Paypal and click on the “Send Money” tab.

You do need to have a Paypal account to use this feature. If you don’t have a PayPal account, it is easy to sign up for one. Go to www.paypal.com and indicate that you want to send money to: scwt_bellamia@yahoo.com. Indicate the amount you would like to give to the Colony Dogs. You can pay by credit card. Use PayPal to send money in US currency in any denomination that you wish.

I will personally absorb all the transaction fees involved, so your entire gift will be sent to the Colony Dogs.

FOR CHECKS: Tonya said it is best to make a check made payable to her because many of the places where she purchases grooming supplies for the Colony Dogs will not accept a purchase order from NCSU, and it takes a while for Tonya to get reimbursed from NCSU when she pays for these items out-of-pocket. Tonya also shops at places like Petco and Petsmart for Nylabones for the Colony Dogs, and they also will not accept purchase orders there for purchases.

You may send your check made payable to TONYA HARRIS at the address above for Tonya.

Tonya can guarantee that whatever amount you send her, she will make sure that the Wheatens and Wheagles will get great presents for the holidays!

If the Colony Dogs could speak, they would say “Thank you for caring about us!”

www.colonydogs.org

“Colony Dogs. . .we care!”
TEST! TEST! TEST!

Please remember to test your Wheaten, at least annually. Our health researchers currently recommend that annual testing include a Complete Blood Count (CBC), Super Chemscreen, Urinalysis, and Urine Protein:Creatinine Ratio. Additional screening tests available include the Heska ERD Test, the MA (microalbumin) Test, and the Fecal API Test. Printable Testing Protocols designed for Wheaten owners and also for their Veterinarians can be found on the SCWTCA website at [www.scwtca.org](http://www.scwtca.org/).

Retest your Wheaten according to your Veterinarian’s advice, if any result presents cause for concern.

It is essential that you track your Wheaten’s test results and watch for any trends. Early diagnosis of all health problems, including but not limited to kidney issues, is vital for a positive prognosis.

An easy-to-use, online Health Tracker is available through a $10 donation to the SCWTCA Endowment Fund ([www.wheatenhealthendowment.org](http://www.wheatenhealthendowment.org)). Please send your donation to SCWTCA Endowment Fund, c/o Rosemary Berg, Endowment Secretary/Treasurer, 37953 Center Ridge Drive, North Ridgeville, OH 44039-2821. You can get the Health Tracker by emailing Anna Marzolino at marzolinoam@aol.com. Anna is also available to help with any questions on how to input data onto the Health Tracker.

DONATE TO SCWTCA HEALTH ENDOWMENT

The Board of the Soft Coated Wheaten Terrier Club of America and the Endowment Board thank everyone for their generous donations. Donations either fund grants selected by the SCWT Endowment Fund Board or provide matching funds for grants approved by the American Kennel Club/Canine Health Foundation (AKC/CHF).

Send your contribution to Rosemary Berg, 37953 Center Ridge Dr., North Ridgeville, OH 44039-2821.

Make check payable to SCWTCA Endowment (US funds only), or contribute online via the website [www.wheatenhealthendowment.org/endowmentform.html](http://www.wheatenhealthendowment.org/endowmentform.html).

DONATE TO AKC/CHF SCWT GENETIC RESEARCH FUND

The Board of the SCWT Genetic Research Project thanks everyone for their generous donations to the fund.

The SCWT Genetic Research Fund, in cooperation with the AKC/CHF, sponsors genetic research into the canine genome, specifically aimed at identifying the genes responsible for the transference of PLE/PLN. This information will make it possible for the development of testing protocols to identify Wheatens with protein-wasting diseases.

To join our effort with a tax deductible donation, make your check payable to AKC/CHF SCWT Genetic Research Fund and mail to: David Ronsheim, Project Financial Officer, 17827 Fireside Drive, Spring, TX 77379-8017.

Or, visit our website ([www.scwtgrf.com](http://www.scwtgrf.com)) to make an online donation through PayPal.