currently holds 900 DNA samples and 550 x-rays. Dogs in the database are identified by number only, making their identities "as confidential as your Visa information or your bank balance is at the bank," and their pedigrees are checked through a DNA matrix.

The database can be used to study two types of disease, Dr. Lark explained. Simple diseases, usually recessive and controlled by one gene, include PRA and cardiomyopathy in Portuguese Water Dogs. The more complex diseases, all of which depend on multiple genes, include cancer, autoimmune disease, and osteoarthritis. Once the canine genome was sequenced, it became possible to identify the genes in the Water Dog that control its size and shape and differentiate individuals between the two classic shapes—long, thin legs and long snout, or a more powerful build comparable to a bulldog.

The ability to identify genes or gene clusters that regulate body size and shape helped explain how different dog breeds arose so quickly, he said: "There were massive clusters of genes that could move whole shape and functional differences." Genetic research on the Water Dogs has also identified one gene for osteoarthritis and two for Addison's disease, one that increases frequency and one that decreases it.

Future research will be much easier, now that the breed's genetic sequence has been mapped. "Every time you get a new phenotype, a new characteristic, a new disease, you can plug it in and you already have the genetic information," he explained. "So once that investment has been made, you have an enormously powerful tool. And you want to strike while the iron is hot, while those dogs are still there." With that in mind, owners participating in the Georgie Project are being asked for blood samples, and they will also be asked to participate in an autopsy program as their pets die.

"Emotionally and financially this is a tremendous venture," he said. "But if we can autopsy as many as 300 of these 500 dogs, we will know their state of health at the time of death." An initial series of about 15 autopsies has already identified a dog with cancer that had preclinical irritable bowel disease [editorial note: I think he said IBD], and a dog with Addison's that also suffered from autoimmune polyglandular syndrome. "If we can correlate these, we may be able to get some idea for early diagnosis."

For other breeds, Dr. Lark warned that even simple recessive diseases take time to study. More complex, cutting-edge diseases are "much more expensive, and take a much longer time to pay off. But if you don't start now, you'll never get there." The Georgie Project has collected more than $1 million over the past nine years, and was very fortunate to benefit from a $200,000 seed grant that called for quantitative research on plants or animals.

Corporate sponsors and the National Institutes of Health are now taking an interest in the project, even though NIH decision-makers are still much more interested in mouse models. But "now that the dog genome has been sequenced, there are a lot of advantages," he said. "The dog has a much closer genome to the human. More than 300 human genetic diseases are found in dogs. The different breeds are genetic isolates, so they're very important and very hard to find in humans." Even with that understanding, the NIH won't fund a project unless a breed club has signed on.

Dr. Lark challenged the view that breeders should attempt to eliminate chromosomal aberrations once they have been isolated. "As a scientist, I tell you that if you do that, you're throwing the baby out with the bathwater, because you have no idea what other genes may be linked," he said. "It may be the gene for the most beautiful coat you've ever seen, or it may be for the shape of the dog or the behavior." The alternative is to be sure that carrier dogs are bred with normals, rather than ruining a breed in an attempt to perfect it.

CANINE AUTOIMMUNE THYROID DISEASE AND SYMPTOMS OF HYPOTHYROIDISM

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CANINE AUTOIMMUNE THYROID DISEASE: COMMON PROBLEM OF PUREBRED DOGS
by W. Jean Dodds DVM

The information provided here outlines an approach that has been used successfully by the author to reduce the prevalence of clinically expressed canine thyroid disease within susceptible families or breeds.

EARLY THYROID DISEASE (THYROIDITIS)
COMPENSATORY AND CLINICAL CANINE HYPOTHYROIDISM

Most of the confusion about the diagnosis and treatment of thyroid disease in purebred or mixed breed dogs today stems from the expectation that affected animals must show clinical signs of inadequate thyroid hormonal production (i.e. hypothyroidism) in order to have the disease. The term hypothyroidism has been loosely applied to describe all stages of this disease process whereas strictly speaking it should be reserved for the end-stages when the animal's thyroid gland is no longer capable of producing sufficient hormone(s) to sustain clinical health. At this point, the dog can express any number of the non-specific multisystem signs of thyroid dysfunction. But let's start at the beginning.

The most common cause of canine thyroid disease is autoimmune thyroiditis (estimated 90% of cases). Thyroiditis is an immune-mediated process that develops in genetically susceptible individuals and is characterized by the presence of antithyroid antibodies in the blood or tissues. Thyroiditis is believed to start in most cases around puberty, and gradually progress through mid-life and old age to become clinically expressed hypothyroidism once thyroid glandular reserve has been depleted. During this process, the animal or person becomes more susceptible to immune-mediated or other diseases affecting various target tissues and organs. The prerequisite genetic basis for susceptibility to this disorder has been in established in humans, dogs and several other species.

The above explanation helps us to appreciate existing confusion and controversy within the veterinary profession regarding whether or not testing or treatment is indicated for dogs that fail to show typical signs of hypothyroidism. In fact, we have only recently begun to recognize the subtle signs of early thyroid dysfunction in dogs as prevalence of the autoimmune form of the condition has increased within and among dog breeds. Today, some 50 breeds are genetically predisposed to develop thyroid disease.

GENETIC SCREENING FOR THYROID DISEASE

These thyroid panels and antibody tests can also be used for genetic screening of apparently healthy animals to evaluate their fitness for breeding. A bitch with antithyroid antibodies in her blood may pass these along to her puppies in her colostral milk. Also, any dog having circulating antithyroid antibodies can eventually develop clinical symptoms of thyroid or other autoimmune diseases. Therefore, thyroid screening can be very important for potential breeding stock.

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 anestrus period for females following their maiden heat). Anestrus is a time when the female sexual cycle is quiescent, thereby removing any influence of sex hormones on baseline thyroid function. 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 is more reliable when they are tested in anestrus. Testing for health screening is performed at 12-16 weeks from the onset of the previous heat. In fact, genetic screening of intact females for other parameters like von Willebrand's disease or wellness health and reproductive checkups should also be scheduled in anestrus females. Once the initial thyroid profile is obtained, dogs and bitches should be rechecked on an annual basis to assess their own health. Annual results permit comparisons that should reveal early evidence of developing thyroid disease or dysfunction. This also allows for early treatment where indicated to abort the development or advancement of clinical signs associated with hypothyroidism.

Healthy young dogs (less than 15-18 months of age) should have thyroid baseline levels for all parameters in the upper 1/2 to 1/3 of the adult normal ranges. In fact, for optimum thyroid function in screening breeding stock, levels should be at least at the midpoint of the laboratory normal ranges, because lower levels may well be indicative of the early stages of thyroiditis among relatives of dog families known to have thyroid disease.

TREATMENT OF THYROID DISEASE

The new information summarized here has changed our approach to treatment and control of thyroid disease. In addition to providing thyroid supplementation for dogs showing the typical signs of thyroid disease, we now know that treatment of dogs showing the early stages of thyroiditis (based on the testing described above) is necessary and important to correct the underlying thyroid imbalance, reduce the risk of developing other related immune-mediated disorders, and to control or prevent the process of thyroiditis from progressing to depletion and exhaustion of the thyroid gland.

1. Type of Treatment

The treatment of choice because of its wide safety margin and efficacy is T4 hormone (L - or levothyroxine). The most commonly used brand names are Soloxine (Daniels) and Synthroid (Flint) and we recommend either of these over generics especially for the smaller breeds. Use of T3 hormone (triiodothyronine) is not recommended for initial use because toxicity can more easily develop with this product; T3 is the intercellular hormone whereas most of T4 must be first converted to T3 before it achieves its metabolic effect. In some cases where the animal's body cannot properly convert T4 to T3, the dog will need both T4 and T3 therapy to correct the problem. For this purpose, the general rule of thumb is to give from 2/3 to a full dose of T4 and a 1/3 dosage of T3 (i.e., 0.1 mg per 10-20 pounds of T4 plus 1 ugm per pound of T3 twice daily). However, no dog should be treated with these thyroid hormonal preparations without having proper veterinary testing, medical examination and follow-up.

2. Frequency of Treatment

Thyroid hormones should always be given twice daily to effect the best response. Until recently, veterinarians have been advised to give treatment to effect either once or twice daily because data on this point was unclear. We now know that the half-life of T4 in the dog is about 10-12 hours (much shorter than humans); for T3, it's only 6-8 hours. Thus, about half of the hormone is metabolized and excreted from the body within 12 hours. Furthermore, twice daily dosing aids in controlling thyroiditis because it shuts off pituitary production of TSH by negative feedback in concert with the half-life of the hormone. In other words, the dog's own thyroid follicular cells become quiescent and are less likely to stimulate production of the antithyroid antibodies responsible for the disease. (Obviously these are simplistic explanations of the complex metabolic, immunologic and biochemical events involved.) Contrary to some popular wisdom, treatment with thyroid hormone does not destroy or suppress the potential of the gland to respond on its own once treatment is stopped for whatever reason. The latest veterinary research shows that it takes the thyroid gland up to 30 days to recover its full potential once therapy is withdrawn. Therefore if an animal has been medicated, where the diagnosis is unclear, treatment should be withdrawn (if it's clinically safe to do so) for 30 days before the animal is retested with the complete type thyroid profile described above

Follow-up testing after initiating treatment is usually performed after four to eight weeks of therapy. The sample should be taken 4-6 hours after the morning dosage and optimum results will show thyroid values in the upper third of normal ranges at the peak time of absorption. Dosage can then be adjusted accordingly if needed. Dogs on long term therapy with thyroid hormones should be monitored with complete panels (not just T4 as you need to be sure the dog's body is converting the T4 medication properly to T3) on a regular basis (every 6-12 months).

CLINICAL SIGNS OF CANINE HYPOTHYROIDISM

<u>Alterations in Cellular Metabolism</u>
weakness / stiffness / laryngeal paralysis / facial paralysis / tragic expression / knuckling or dragging feet / muscle wasting / megaesophagus / head tilt / drooping eyelids

<u>Neuromuscular Problems</u>
seizures / mental dullness / exercise intolerance / neurologic signs polyneuropathy / lethargy / weight gain / cold intolerance / mood swings hyperexcitability / stunted growth / chronic infections

<u>Dermatologic Diseases</u>
dry, scaly skin and dandruff / coarse, dull coat / bilateral symmetrical hair loss / rat tail, puppy coat / hyperpigmentation / seborrhea or greasy skin pyoderma or skin infections / myxedema / chronic offensive skin odor

<u>Reproductive Disorders</u>
infertility of either sex / lack of libido / testicular atrophy / hypospermia aspermia / prolonged interestrus interval / absence of heat cycles / silent heats / pseudopregnancy / weak, dying or stillborn pups

<u>Cardiac Abnormalities</u>
slow heart rate (bradycardia) / cardiac arrhythmias / cardiomyopathys

<u>Gastrointestinal Disorders</u>
constipation / diarrhea / vomiting

<u>Hematological Disorders</u>
bleeding / bone marrow failure / low red blood cells / low white blood cells / low platelets

<u>Ocular Diseases</u>
corneal lipid deposits / corneal ulceration / uveitis Keratococonjunctivitis / sicca or dry eye / infections of eyelid glands (Meibomian gland)

<u>Other Associated Disorders</u>
lgA deficiency / loss of smell (dysosmia) / loss of taste / glycosuria / chronic active hepatitis / other endocrinopathies adrenal, pancreatic, parathyroid