Thyroid Problems of the Basenji Dog

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Autoimmune Lymphocytic Thyroiditis – The Unknown Epidemic?? © 2005
Written by sinbajé basenjis for the BCOA Bulletin - a quarterly publication of the National breed club

Surveys conducted in the mid 1990's by the AKC Delegate Committee on Health Research showed thyroid disease to be the number one health concern of major breed clubs, placed ahead of hip dysplasia and epilepsy in breeds with a high incidence of both. Due to this overwhelming concern, thyroid testing, diagnosis and treatment have improved tremendously over the years. However, when compared to fanconi, malabsorption, or PRA, thyroid dysfunction fails to ignite much interest in the basenji breed. The thyroid is treated much like a poor relation, greatly ignored by the breeding masses, despite our ability to test for this hereditary condition early and often. Are we doing the breed a major disservice by not taking thyroid disease in breeding stock more seriously?

What is the exact function of the thyroid and why is proper function so important?

The sole purpose of the thyroid gland is to convert dietary iodine into two thyroid hormones; thyroxine (T4) and triiodothyronine (T3). Once converted, these hormones are dispersed throughout the body where almost every cell depends upon them for regulation of their individual metabolism. This means excessive, sufficient or insufficient thyroid levels affect every metabolic activity of the body to some degree, either positively or negatively.

When thyroid hormones become abnormal, many, if not all, body systems are also affected; skin (hair), immune system (allergies), sex glands (low sex drive and/or infertility) and brain (seizures and/or aberrant behavior such as aggression) to name just a few. Proper thyroid function is needed for proper body function. Too much thyroid hormone, or hyperthyroidism, means metabolism speeds up. Too little thyroid hormone, or hypothyroidism, means metabolism slows down. Hyperthyroidism, while quite common in the cat, is extremely rare in the dog while the opposite is true of hypothyroidism; rare in the cat and common in the dog. Research has shown the most common disease of the canine endocrine system to be primary hypothyroidism.

What exactly is hypothyroidism and how is it diagnosed?

In short, active hypothyroidism (HT) is created when the thyroid gland is no longer efficient at converting iodine into much needed thyroid hormone (T3 and T4) and body systems begin to wane. The most accurate means of diagnosis is made via a series of specific blood tests, with or without correlating symptoms. Symptoms can range from the outwardly obvious – weight gain, lethargy and behavior changes to inwardly subtle – anemia, and sterility and have been shown to take as long as 18 months after the official lab diagnosis to become noticeable. While hypothyroidism can be diagnosed via blood work without supporting symptoms, an influx of symptoms is not always predictive of hypothyroidism, as there are many other conditions with parallel symptoms.

There are three classifications of hypothyroidism: primary, secondary and tertiary with primary being associated with the thyroid gland, secondary with the pituitary gland and tertiary with the hypothalamus. As previously stated, primary hypothyroidism appears to have a high rate of occurrence in the canine with secondary and tertiary being less commonly found. While there are five classes of primary canine hypothyroidism, the two most commonly found are: autoimmune lymphocytic thyroiditis (ALT) and idiopathic follicular atrophy. While hypothyroidism is not a life threatening condition when properly treated, the quality of life for a true hypothyroid animal, especially one not accurately diagnosed and/or treated, can be substandard.

What is Autoimmune Lymphocytic Thyroiditis (ALT)?

Autoimmune Lymphocytic Thyroiditis (ALT) is a hereditary disease that occurs when lymphocytes, or white blood cells associated with the immune system, attack the thyroid gland creating inflammation. The lymphocytes not only attack, they irreversibly destroy healthy thyroid tissue needed to produce thyroxine (T4), the hormone that supports body system metabolism. Without viable tissue, the gland can no longer produce T4 and the dog becomes actively hypothyroid. While ALT is responsible for 50% of all primary hypothyroid cases, active hypothyroidism is not a guaranteed outcome of all ALT diagnosis. The Orthopedic Foundation for Animals (OFA), a national health registry, classifies ALT in two ways: positive advanced or compensative.

- Positive advanced ALT occurs after total eradication of all thyroid tissue and is defined by the following lab results: positive

TgAA, low FT4(ed), and high cTSH.

A dog with positive advanced ALT is by all accounts actively hypothyroid and should begin hormone replacement therapy even though clinical (observable) symptoms may take as long as 18 months to support lab work. This lack of symptoms can be deceiving, making some owners unwilling to medicate immediately. This is a mistake.

- Compensative ALT is when inflammation of the thyroid gland is still in the early stages and complete destruction of the gland has not yet occurred. It is defined by the following lab results: positive TgAA, normal FT4(ed), and normal cTSH.

While compensative ALT dogs do have a high probability of progressing to active hypothyroidism, especially when positive T3AA and T4AA are also present, active hypothyroidism does not always occur, making hormone therapy of compensative ALT dogs debatable/controversial in some circles. Retesting compensative dogs semi-annually, to keep abreast of any lab work changes that might indicate a development to active hypothyroidism, and supplementing at that time, is a viable option for those owners who do not feel comfortable medicating.

Canine ALT shows no gender inclination with both sexes being equally at risk. ALT is considered to be hereditary and is believed to be polygenetic with familial tendencies, much like hip dysplasia, though some experts feel it is more autosomally recessive in nature. Therefore, dogs diagnosed with either positive advanced or compensative ALT (or positive TgAA) should be bred carefully, if at all.

What is "idiopathic follicular atrophy hypothyroidism"?

Idiopathic atrophy of the thyroid gland is characterized by the unexplained loss of thyroid cells, which are replaced by fat and/or scar tissue. Once again, the lack of functioning thyroid cells needed to produce thyroxine (T4), is what creates active hypothyroidism. While idiopathic loosely means 'without cause', research is beginning to suggest that 50% of diagnosed idiopathic atrophy is more likely a natural progression, or end result, of the heritable autoimmune lymphocytic thyroiditis. This translates to roughly 75% of true thyroid disease being caused in some way by ALT, a hereditary condition. The remaining 25%, those that are truly idiopathic 'without cause', appears to be quite rare in young dogs, affecting most dogs in mid-life between the ages of 5 and 9, and is not believed to be hereditary. That said, true idiopathic hypothyroidism should not be considered a "common" condition of a specific breed.

What does FT4(ed), cTSH, TgAA, et al mean – it's all Greek to me?

T4 (thyroxine) is one of two thyroid hormones used in the regulation of the body's metabolism. FT4(ed), sometimes seen as FT4D, stands for free thyroxine tested by way of equilibrium dialysis. Free, to mean not bound by carrier protein representing the portion of the T4 hormone that is actually active on a cellular level, as opposed to representing all parts that make up the total T4. Use of the equilibrium dialysis testing method is considered as the 'gold standard' due to its lack of interference by T4 autoantibodies (T4AA) as the process of dialysis actually removes said antibodies during testing. The radioimmunoassay (RIA) method of testing can have T4AA interference, which simply means that the interference must be taken into consideration when FT4 (RIA) results are interpreted as T4 levels can be falsely increased or decreased depending on the lab running the test.

cTSH is canine thyroid stimulating hormone. The job of the cTSH is to regulate the production of T4 within the thyroid gland, much like a thermostat regulates whether the furnace should heat up, cool down or stay as it is. When T4 circulation levels drop, the pituitary gland is alerted to the problem and quickly responds by releasing cTSH, which makes its way to the thyroid gland where it attempts to stimulate the gland into producing more thyroxin (T4). In theory, when the T4 level is normal, cTSH is expected to also be normal. When T4 levels are high, cTSH is expected to be low, as there is no need for more T4 in the system and once cTSH production is stopped, its levels decrease. When T4 levels are low, cTSH is expected to be high, as the pituitary gland is hard at work making cTSH needed to encourage the thyroid into increasing its T4 production. While the TSH test in humans has a near 100% rate of accuracy, the canine TSH is less precise with an accuracy rate closer to 85%, meaning that a small percentage of hypothyroid dogs may not show the expected elevation in serum TSH. This low diagnostic sensitivity understandably keeps some testing facilities from incorporating the cTSH into their diagnostic profiles, however increased diagnostic differentiation between those animals who are sick, but have normal functioning thyroids, and those with active hypothyroidism, has been found when cTSH is used along with FT4ed and TgAA.

TgAA is short for thyroglobulin autoantibodies and is believed to be the first indicator of hereditary autoimmune lymphocytic thyroiditis. TgAA can be positive a year or two before clinical signs are noted, which allow breeders to test early and often so that

better breeding decisions can be made which will ultimately reduce the prevalence of the disease within the breed. The standard methodology of TgAA testing is via enzyme-linked immunosorbent assays (ELISA). The ELISA test has been compared favorably with thyroid biopsy results, which is to say, when ELISA results have said "positive", corresponding thyroid biopsy results have also said "positive". Testing via the ELISA method is considered by some to be the 'gold standard' of genetic screening for ALT. Note of interest: It has been recently identified that statistically, significantly higher prevalence of positive TgAA has been found in, amongst several other breeds, the basenji dog.

T3AA/T4AA is T3 and T4 autoantibodies respectively. Autoantibodies are proteins produced by the immune system against its own tissues which are perceived as foreign invaders. Defined as TgAA subclasses, both T3AA/T4AA are considered, along with TgAA, as markers for ALT. While almost all cases of autoimmune lymphocytic thyroiditis will have elevated TgAA levels, less than 20% of these same cases will also have elevated T3AA or T4AA. Since the absence of T3AA/T4AA has a high rate of expectancy (~80%), nothing diagnostic, specifically idiopathic hypothyroidism should ever be inferred by the lack of their presence when FT4ed is low and TgAA is either negative or untested. Human thyroid articles suggest that T3/T4 AA levels, especially T3AA, can be falsely elevated due to interference from lipids (fat) in the serum or blood cell damage due to processing and are therefore not routinely included in human thyroid testing panels. However, T3AA/T4AA testing is important in animal diagnostics, especially when radioimmunassay (RIA) method of testing is used to measure T3 and T4, due to their ability to interfere with (falsely increase) the results. Accurate interpretations of RIA based T3 and T4 results can not be fully established without first knowing whether or not T3/T4 autoantibodies are also present.

Do I understand this right? If my dog is TgAA negative then I'm in the clear?

Unfortunately it is not so simple. If a dog's TgAA is tested for the first time at the age of five and the TgAA is negative it can not be said, with 100% certainty, that the dog did not, in the proceeding five years, have positive TgAA, and thus hereditary autoimmune lymphocytic thyroiditis. The recommendations for properly screening breeding stock of hereditary autoimmune lymphocytic thyroiditis is to start testing at the age of one. Test annually until the age of five, then every other year until old age. Studies have suggested that a dog tested annually from the age of one who does not acquire the disease by the age of five, has a greater potential of remaining disease free throughout its lifetime. That said, there are cases, albeit rare, where TgAA initially becomes positive beyond the age of five due perhaps to a disruption of the gland structure or thyroid tumor rather than inflammation normally associated with autoimmune lymphocytic thyroiditis.

Isn't active hypothyroidism the same as autoimmune lymphocytic thyroiditis (positive TgAA)?

No. Autoimmune lymphocytic thyroiditis, or positive TgAA, is merely a classification of thyroid damage; it alone doesn't tell us whether thyroid function has (yet) been affected. While autoimmune lymphocytic thyroiditis is the major cause (~75%) of active hypothyroidism, many dogs can harbor thyroiditis for years before showing clinical (observable) signs of the disease, if at all. It is believed that 60% or more of viable thyroid tissue needs to be destroyed before lab work begins to reflect thyroid dysfunction. Studies have shown that there is no set rule to the development, or lack of development, of autoimmune lymphocytic thyroiditis as some dogs remain TgAA positive for life and never progress to active hypothyroidism, while others become actively hypothyroid and need hormone supplementation. Some dogs go from positive to negative TgAA and still have enough viable thyroid tissue needed to produce adequate amounts of T4, while other dogs will go from positive to negative TgAA and have no functional tissue left and become actively hypothyroid and in need of supplementation. Regardless of whether the dog does or does not progress to active hypothyroidism the fact remains that if the TgAA is positive the dog has hereditary autoimmune lymphocytic thyroiditis and should not be bred.

What's the big deal? It's not like hypothyroidism can kill my dog.

Hypothyroidism that has not been properly diagnosed does have the potential to directly and/or indirectly kill your dog or a dog you have bred. The ultimate consequence of hypothyroidism can result in coma (myxedmatous coma). The immune system does not function correctly as a result, leaving the dog susceptible to infections and blood poisoning. Fatal anaphylactic reactions to spider bites, ingested plant material and/or of unknown origins are common problems in the canine species. Thyroid dysfunction comprises the immune system leaving a dog susceptible to these kinds of deadly allergic reactions.

Puberty, roughly between fifteen and eighteen months of age, is a prime time for basenjis to exhibit aberrant behaviors such as aggression. Many pet owners, too embarrassed to contact their breeders, feeling perhaps they did something wrong in the pups upbringing, choose instead to dump the "problem" dog onto their local animal shelter. On a good day the shelter might contact purebred rescue and have the animal picked up where it will be evaluated and hopefully re-homed. On a bad day the 'aggressive' basenji, a breed already labeled as 'land sharks' in the animal care profession, has a high probability of being euthanised to make room for a more adoptable dog. The more tenacious owner might keep the aggressor longer, perhaps spending a fair wage on behavior modification training, to no avail, while continuing to live in fear of their highly unpredictable pet. Eventually they too release the dog where death is not always last on the list of probabilities, and thyroid testing is rarely, if ever, first.

While hypothyroidism might not seem like a big deal to breeders when compared to other ills of our breed, it becomes a big deal to the average pet owner, who has the most to lose, financially and emotionally. All breeders should be actively trying to produce the best dogs and should therefore be concerned about thyroid disease. While hypothyroidism is easily treated, and the medication is relatively cheap, the cost of initial diagnosis can run into the high hundreds for those dogs showing symptoms of a number of other possible conditions, using common veterinary practitioners unfamiliar with current thyroid testing protocols. Add to that the life sentence of annual testing, at times semi-annually, and you are looking at serious monetary investments for a disease that can be controlled by breeders through proper screening and culling of breeding stock.

What can I do as a breeder?

The following suggestions for reducing the incidence of hereditary primary hypothyroidism was cited from the International Symposium of Canine Hypothyroidism at the University of California - Davis:

- Keep accurate records of thyroid status, especially parents, siblings and offspring.

Much like hip dysplasia, vertical pedigrees have more information for breeders evaluating gene potential when compared to the more standard horizontal pedigrees. The premise being that a dog that has several affected littermates has a greater potential for carrying the disease than a dog whose maternal grandmother is the only dog affected. Keeping track of all siblings and offspring - even those sold as pets - is crucial in creating these informative vertical pedigrees.

- Expand gene pools by avoiding inbreeding and line breeding.

This is especially true for basenji families with a large number of dogs on thyroid hormone supplementation. The prevalence of familial hypothyroidism has been shown to decrease with each generation when dogs symptomatic for hypothyroidism are removed from breeding.

- Remove TgAA positive dogs from the breeding pool

In order for this to work to its full potential, TgAA must be tested annually from the onset of puberty, around the age of one, to the age of five and then every other year. Breeding of dogs should ideally not take place until after the age of five, with three being the absolute minimum age. If the TgAA has not been tested from the onset, hereditary status is not fully known and care should be taken by way of current testing along with close study of vertical pedigrees of potential sires and dams for risk factors such as numerous hypothyroid siblings/offspring/aunts/uncles.

Is there a time when my dog should/should not be tested?

The blood sample should be taken when the dog is relaxed and otherwise healthy, is not approaching or in a heat cycle, and is not being medicated with the following, due to their ability to falsely decrease T4 levels; steroids, non-steroidal anti-inflammatories, sulfonamides or anti-seizures. If in doubt, including cTSH levels in your testing regime might provide a clear distinction between true hypothyroidism and drug suppression.

A dog whose hypothyroid diagnosis is questionable, but is currently on thyroid replacement therapy, should discontinue medication for at least 6 weeks prior to testing so that the dog's true thyroid function will not be influenced by the medication.

Tell me again the tests I should be asking for.

Ideally a full thyroid profile - FT4ed, cTSH, TgAA, T3AA & T4AA will show every piece of the puzzle needed for accurate diagnosis: T4/cTSH to show thyroid dysfunction, if any and TgAA/T3AA/T4AA to show hereditary disease, if any. However, doing a full profile, every year from the age of one onwards, on every breeding animal is not cost effective for most breeders. Another approach would be to test only the TgAA during the first four years, adding the full panel at the age of five and then testing every other year from then onwards. Should the TgAA become positive prior to the age of five a full panel is necessary to get a baseline level of the thyroid function. Since relatively few dogs have been shown to have low T4, high cTSH and negative TgAA prior to the age of five, testing TgAA only would be a cost efficient means of hereditary screening.

Where can I get tested?

Diagnosing hypothyroidism solely on total T4 (TT4) blood levels and ambiguous clinical signs, is considered archaic by most experts in the field and yet many local practitioners continue to do just that. Until all veterinarians educate themselves on current testing recommendations, it is suggested that outside laboratories be used for more accurate thyroid screening.

Whether you are interested in testing for OFA certification, or for your own records, the following are approved OFA thyroid testing facilities. Applications for OFA certification, along with their fees, can be found at: (http://ofaweb.offa.org/OFA)

Note: For inclusion to the OFA registry FT4ed, cTSH and TgAA are the only tests needed. However, as stated above, a full thyroid profile should ideally include FT4ed, cTSH, TgAA, T3AA & T4AA. All testing facilities listed below can do a full panel if requested.

Animal Health
Diagnostic Lab
Michigan State University
517-353-0621

Veterinary Diagnostic
Laboratory
Univ. of Minnesota
612-625-6782

Diagnostic
Laboratory
Cornell Univ.
New York
607- 253-3673

Vita-Tech
Ontario CANADA
1-800-667-3411

University of California
Veterinary Medical
Teaching Hospital
530-752-7380

Texas Veterinary Medical
Diagnostic Lab
Texas A&M
979-845-3414

Animal Health
Laboratory
Ontario CANADA

519-824-4120
ext.54501

Veterinary
Diagnostic Lab
University of
Minnesota
612-624-0761

Antech Diagnostics*
Lake Success , NY
800-872-1001

Be sure to check with each referral laboratory individually for special sample handling of tests for OFA registry purposes.

*only the Lake Success, NY location of Antech has been certified to process OFA thyroid panels

HEMOPET is another good testing facility that not only offers a wide range of testing and vaccine titration, but also the chance to personally discuss the results and/or treatment needed with the attending veterinarian, Dr. W. Jean Dodds. Being a small, not for profit blood bank, HEMOPET has not applied for OFA accreditation due, in part, to the substantial fee needed for application. Test request forms and instructions can be found at: http://www.itsfortheanimals.com/HEMOPET.HTM

HEMOPET: Dr. W Jean Dodds, DVM
11330 Markon Drive
Garden Grove, CA 92841
Phone: 714/ 891-2022

PLEASE NOTE: Because HEMOPET does not include TgAA in their Thyroid Antibody Profile, or Free T4 by equilibrium dialysis, you must ask for these tests specifically if you are interested in them.

If there were any keys points to remember – what would they be?

There are currently forty-four (44) basenjis registered with the OFA Thyroid registry. Of these, 15.9% have been diagnosed as having hereditary autoimmune lymphocytic thyroiditis. For comparison purposes, percentages for the top three breeds showing the highest prevalence of thyroiditis per the OFA website were: 22.1.4%, 20.3% and 14.6% respectively. MSU shows 12.4% of all basenjis tested as having thyroiditis, with another 7.7% needing to be retested due to questionable (non definitive) results. Basenjis ranked 28 out of 100 breeds represented for prevalence of thyroiditis. Another interesting comparison would be versus the evidence of hip dysplasia in the basenji; per OFA only 2.8% of the 1436 tested had abnormal hips. That's 2.8% hips versus 15.9% ALT. Ironically, breeders are more concerned with hips than they are thyroids!

Ideally a full thyroid profile - FT4ed, cTSH, TgAA, T3AA & T4AA will show every piece of the puzzle needed for accurate diagnosis. However, TgAA is the first indicator of hereditary autoimmune lymphocytic thyroiditis and can be tested for as early as one year of age.

While autoimmune lymphocytic thyroiditis (positive TgAA) is considered to be hereditary and some experts feel dogs diagnosed with positive TgAA should be removed from the breeding pool, there are those who feel that it is a recessive gene and bred wisely, can

be avoided.

~75% of all primary thyroid disease is caused by autoimmune lymphocytic thyroiditis, a hereditary condition while true idiopathic hypothyroidism accounts for roughly 25%. Therefore idiopathic hypothyroidism should not be a "normal" condition in any breed.

Hereditary autoimmune lymphocytic thyroiditis can NOT be definitively ruled out if the dog's TgAA was initially tested negative at the age of five due to the lack of information in the proceeding five years.

The prevalence of familial hypothyroidism has been shown to decrease with each generation when dogs symptomatic for hypothyroidism are removed from breeding.

Symptoms can take as long as 18 months after lab work supports active hypothyroidism to become noticeable, making blood work crucial for early accurate diagnosis.

All breeders should be actively trying to produce the best dogs and should therefore be concerned about thyroid disease.

Personal Acknowledgments:

Dr. Peter A Graham BVMS, PhD, CertVR, Diplomate ECVCP, MRCVS
Director North Western Laboratories and Cambridge Specialist Laboratory Services, UK
Dr. Graham worked in the thyroid lab at Michigan State University (www.ahdl.msu.edu) for 7 years before moving recently to head two British based laboratories, North Western Laboratories (www.nwlabs.co.uk) and Cambridge Specialist Laboratory Services (www.cslabs.co.uk) and has authored/co-authored numerous peer reviewed articles relating to thyroid function and testing.

Dr. W. Jean Dodds, DVM
Dr. Dodds, is a nationally and internationally recognized authority on blood and immune disorders, thyroid disease and nutrition. Dr. Dodds is the president of Hemopet/Pet Lifeline, the first national nonprofit animal blood bank and greyhound rescue/adoption program serving North America. Hemopet also conducts nonprofit clinical research studies.

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http://www.endocrineweb.com/tests.html
Thyroid Function in Dogs: MSU FAQs:
http://www.dcpah.msu.edu/Labs/Endocrinology/FAQ/thydogs.htm