# THYROID TESTING

Hypothyroidism is the most common endocrine disorder of canines.

At least 80% of cases result from autoimmune thyroiditis. The heritable nature of this disorder poses significant genetic implication for breeding stock. Thus accurate diagnosis of the early stages of canine autoimmune thyroiditis leading up to hypothyroidism provides important genetic and clinical options for prompt intervention and case management.
Puppies tend to have higher basal thyroid levels than adults, and geriatrics tend to have lower basal thyroid level than adults. Dogs fed gullet or throat portion of raw red meat may have iatrogenic hyperthyroidism due to the excess amount of thyroid hormone not only in the meat source, but also in the juices from the meat. Removing the meat from the diet resolves the hyperthyroidism in about 4-6 weeks and basal levels return to normal. Feeding excessive amounts of iodine in foods and supplements (kelp, seaweed) reduces the thyroid function. This contributes to the rising prevalence of hypothyroidism in young dogs. Iodine also increases auto-antigenic potency of thyroglobulin leading to induction of autoimmune thyroiditis.

It is recommended that dogs be tested after 10-14 months of age in males and during the first anestrous period for females following their maiden heat. Testing annually is recommended for the first four years. After that, testing every other year is recommended. The registry data can be used by breeders in determining which dogs are best for their breeding program. Knowing the status of the dog and the status of the dog's lineage, breeders and genetic counselors can decide which matings are the most appropriate for reducing the incidence of autoimmune thyroiditis in the offspring.

A bitch with circulating thyroid autoantibodies has the potential to pass these along to the puppies transplacentally as well as via the colostrum. Furthermore, any dog having thyroid autoantibodies may eventually develop clinical symptoms of thyroid disease and/or become susceptible to other autoimmune diseases. Thyroid screening is thus very important for selecting potential breeding stock.Individuals genetically susceptible to autoimmune thyroid disease may also be more susceptible to immune-mediated diseases affecting other target tissues and organs, especially the bone marrow, liver, adrenal glands, pancreas, skin, kidney, joints, bowel and CNS. The resulting "polyglandular autoimmune syndrome" of humans is becoming more commonly recognized in the dog. The syndrome tends to run in families and is believed to have an inherited basis. This multiple endocrnopathy often occurs in patients with underlying autoimmune thyroid disease and concurrent Addison's disease, diabetes, reproductive failure, skin disease and alopecia, and malabsorption syndrome. The most common non endocrinologic autoimmune disorders associated with this syndrome are autoimmune hemolytic anemia (AIHA), idiopathic thrombocytopenic purpura (ITP), chronic active hepatitis, and immune –complex glomerulonenphritis (Systemic lupus erythematosus – SLE). The Nova Scotia Duck Tolling Retriever is listed as one of the breeds genetically predisposed to thyroiditis and Addison's disease.
Aberrant behavior starting around the time of puberty or as young adults has also been associated with thyroid dysfunction. Signs and symptoms include unprovoked aggression, sudden onset of seizure disorder, moodiness, periods of hyperactivity, hypo attentiveness, fearfulness and phobias, anxiety, and submissiveness.

The presence of elevated TgAA, T3 and/or T4AA confirms the diagnosis of autoimmune thyroiditis. Affected dogs should not be used for breeding.

The Orthopedic Foundation for Animals provides certification for dogs that are tested for evidence of Hypothyroidism http://www.offa.org/thy_info.html

OFA will only accept results from approved labs http://www.offa.org/thy_labs.html

This form http://www.offa.org/pdf/thyapp_bw.pdf completed by your veterinarian must accompany all blood samples submitted to the approved lab for OFA Thyroid Panel tests.

For more information and further details on these facts, please refer to the following article by Dr. Jean Dodds of Hemopet:

# PRACTICAL UNDERSTANDING OF THYROID DISEASES & THEIR MANAGEMENT

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## INTRODUCTION

Hypothyroidism is the most common endocrine disorder of canines, and the second most common endocrine disorder of older felines, after diabetes. At least 80% of canine cases result from autoimmune (lymphocytic) thyroiditis). The heritable nature of this disorder poses significant genetic implications for breeding stock. Thus, accurate diagnosis of the early compensatory stages of canine autoimmune thyroiditis leading up to hypothyroidism affords important genetic and clinical options for prompt intervention and case management.

Although thyroid dysfunction is the most frequently recognized endocrine disorder of pet animals, 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 manifestations. Many clinical signs mimic those of other causes and so recognition of the condition and interpretation of thyroid function tests can be problematic (Table 1).

In cats, it has recently been established that feline hyperthyroidism in readily induced, especially in geriatric cats, by feeding commercial pet foods, treats and snacks containing excessive amounts of iodine. This finding has lead to a major change in the iodine formulations of feline commercial pet foods. Hypothyroidism, while rare in cats, can occur in adult cats and a familial hypothyroidism has been described in neonatal Siamese kittens.

### Baseline Thyroid Profiles

A complete baseline thyroid profile is measured and typically includes total T4, total T3, free T4, free T3, T3AA and T4AA, and can include cTSH and/or TgAA. The TgAA assay is especially important in screening breeding stock for heritable autoimmune thyroid disease.

The normal reference ranges for thyroid analytes of healthy adult animals tend to be similar for most breeds of companion animals. Exceptions are the sighthound and giant breeds of dogs which have lower basal levels. Typical thyroid levels for healthy sighthounds, such as retired racing greyhounds, are at or just below the established laboratory reference ranges, whereas healthy giant breeds have optimal levels around the midpoint of these ranges.

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.

<u>All animals are not the same</u>

- Puppies have higher basal thyroid levels than adults
- Geriatrics have lower basal thyroid levels than adults
- Large/giant breeds have lower basal thyroid levels

- Sighthounds have much lower basal thyroid levels

**Dietary-Induced Hyperthyroidism in Dogs and Cats**

Recent studies have documented iatrogenic hyperthyroidism in **dogs** fed the gullet or throat portion of raw red meat (usually beef or lamb). The patient may be relatively asymptomatic or even found to exhibit primary anestrus, with the diagnosis made upon finding significantly high thyroid basal levels without clinical evidence of a thyroid mass in the neck or chest. Questioning of the pet owners then revealed the raw meat diet (owners may not be aware of the portion of the carcass included in the fed product). Excessive amount of thyroid hormone have been measured not only in the meat source, but also in the juices from the meat. Removing the meat from the diet resolves the hyperthyroidism in about 4-6 weeks, and basal thyroid levels return to normal.

With respect to **cats,** the rising incidence of hyperthyroidism in older cats since first identified in the mid-1970s, led to much speculation about the true cause(s). Eventually, research focused on the commercial diets fed to the affected cats; most were found to eat foods containing more than the NRC recommended amounts of iodine. Once the iodine content of the foods was lowered, and even fed in less than the recommended amounts to affected cats, their hyperthyroidism resolved. A prescription diet was produced (Hill's y/d) that contained less iodine for feeding affected cats. Today, a properly balanced amount of iodine is present in commercial pet foods, treats and snacks for both cats and dogs.

Regarding the **iodine content** of commercial pet foods, iodine excess causes alterations in thyroid activity, blocking both its characteristic functions and cell proliferation. Feeding excessive amounts of iodine in foods and supplements (kelp, seaweed) reduces thyroid function in dogs and increases thyroid activity in older cats. This contributes to the rising prevalence of hypothyroidism in young dogs, and hyperthyroidism in older cats. Iodine also increases auto-antigenic potency of thyroglobulin leading to induction of autoimmune thyroiditis.

**Genetic Screening and Diagnostic Testing for Canine Thyroid Disease**

Most cases of thyroiditis have elevated serum TgAA levels, whereas only about 20-40% of cases have elevated circulating T3 and/or T4 AA. Thus, the presence of elevated T3 and/or T4 AA confirms a diagnosis of autoimmune thyroiditis but underestimates its prevalence, as negative (non-elevated) autoantibody levels do not rule out thyroiditis. Measuring TgAA levels also permits early recognition of the disorder, and facilitates genetic counselling (Table 2). Affected dogs should not be used for breeding.

The commercial TgAA test can give false negative results if the dog has received thyroid supplement within the previous 90 days, thereby allowing unscrupulous owners to test dogs while on treatment to assert their normalcy, or to obtain certification with health registries such as the OFA Thyroid Registry. 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 within the previous 30-45 days, or in some cases of non-thyroidal illness. Vaccination of pet and research dogs with polyvalent vaccines containing rabies virus or rabies vaccine alone was recently shown to induce production of antithyroglobulin autoantibodies, a provocative and important finding with implications for the subsequent development of hypothyroidism.

<u>Screening for Canine Thyroid Dysfunction</u>

- Complete thyroid antibody profile preferred

- cTSH poorly predictive (~ 70%) compared to humans
- Age-and breed-specific norms essential for accurate diagnosis; reference lab ranges *not* based on age and breed type
- Basal levels affected by certain drugs (steroids, phenobarbital, sulfonamides, iodine)
- Basal levels lowered by estrogen; raised by progesterone [sex hormonal cycle effects]

Thyroxine Treatment is Best Given Twice Daily

- Dividing the daily dose every 12 hrs avoids "peak and valley" effect
- Achieves better steady state over 24 hrs; half life of T4 is only 12-16 hrs
- Dosing once daily results in undesirable peaks and valleys
- Dosing should be given directly by mouth rather than in food bowl (drug binds to calcium & soy)
- Dispensing thyroxine by human pharmacist often under-doses [dogs need 10 x more]

Testing Dogs on Thyroxine Therapy

- Blood samples should be drawn 4-6 hrs post-pill for BID Rx
- Blood samples drawn 8 hrs post-pill for SID Rx (horses)
- Minimum testing needed is T4 and freeT4
- Thyroid antibody profile preferred; and is required for thyroiditis cases
- Stopping thyroxine to retest basal capacity needs 6 weeks or more
- Thyroid Support or Thytrophin products are inadequate alone to fully correct true hypothyroidism or cannot resolve thyroiditis

A population study of 287,948 dogs published by the MSU Animal Health Diagnostic Laboratory showed that: Circulating thyroid hormone autoantibodies (T3AA and/or T4AA)) were found in 18,135 of these dogs (6.3%). The 10 breeds with the highest prevalence of thyroid AA from their study were: Pointer, English Setter, English Pointer, Skye Terrier, German Wirehaired Pointer, Old English Sheepdog, Boxer, Maltese, Kuvasz, and Petit Basset Griffon Vendeen. Prevalence was associated with body weight and was highest in dogs 2-4 years old. Females were significantly more likely to have thyroid AA than males.

A bitch with circulating thyroid AA has the potential to pass these along to the puppies transplacentally as well as via the colostrum. Furthermore, any dog having thyroid AA may eventually develop clinical symptoms of thyroid disease and/or be susceptible to other autoimmune diseases. Thyroid screening is thus very important for selecting potential breeding stock as well as for clinical diagnosis.

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 anestrus, 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 anestrus. In fact, genetic screening of intact females for other disorders such as von Willebrand disease (vWD), hip dysplasia, and wellness or reproductive checkups (vaginal cultures, hormone testing) is best scheduled during anestrus. 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 to avoid the appearance or advancement of clinical signs associated with hypothyroidism.

Canine autoimuune thyroid disease is very similar to Hashimoto's thyroiditis of humans, which has been shown to be associated with human major histocompatibility complex (MHC) tissue types. A similar association with canine MHC genes in hypothyroid dogs has recently been reported in Doberman Pinschers, English Setters and Rhodesian Ridgebacks, who share a rare dog leukocyte antigen (DLA) class II haplotype which contains a unique DLA-DQA1*00101 genetic determinant. While the presence of this determinant doubles the risk of a dog developing hypothyroidism, it was not found in boxers affected with thyroiditis, nor was it found in the Shih Tzu, Yorkshire Terrier, or Siberian Husky, although more studies are needed in these and other susceptible breeds to establish their true status with respect to this marker DLA antigen. This exciting finding of a common genetic determinant associated with thyroid disease in several breeds hopefully will lead to development of a genetic marker test to identify affected breeding stock and allow for selective breeding to reduce disease incidence in pure-bred dogs.

## Diagnostic Testing for Feline Thyroid Disease

Confusion over the diagnostic utility of the free T4 concentration as measured by equilibrium dialysis (FT4ED) had lead to misdiagnosis of hyperthyroidism in the cat. Use of FT4ED alone as a diagnostic aid (without evaluating a concurrent T4), or as a screening test in healthy cats, has lead to more cats being diagnosed as hyperthyroid than actually have the disorder.

Free T4 is the non-protein bound, physiologically active form of T4 and therefore should be the best marker of thyroid status in dogs and cats. Indeed, in cats with overt hyperthyroidism (consistent clinical signs and high T4), free T4 ED values are elevated. In cats with early or mild hyperthyroidism (more mild signs of disease and T4 in the upper 1/2 of normal reference range), the FT4ED is also usually elevated.

However in 5-10% of cats with non-thyroidal illness (e.g., chronic renal failure, IBD, liver disease, neoplasia) the FT4ED can be elevated for reasons that are unclear. These cats may have signs consistent with hyperthyroidism, (e.g., weight loss, vomiting) but there is typically no palpable thyroid nodule(s), and T4 values are typically within normal limits.

Testing Older Cats

- Basal thyroid levels in older cats should be lower than in adults
- Other illnesses often lower T4, masking hyperthyroidism
- Minimum testing needed is T4, freeT4 and cTSH
- FT4 by ED is usually high in hyperthyroidism but can be high in IBD, renal and liver disease, and neoplasia

### Diagnostic Utility of Canine TSH Assay

Unlike human thyroid function, where the thyroid stimulating hormone (TSH) level gives a diagnostic prediction of primary hypothyroidism with 95% accuracy, the parallel test in dogs (cTSH) results in only ~70% accuracy, because the dog has a more active alternate thyroid regulatory pathway through growth hormone. In addition to this high incidence of false-negative results, cTSH levels appear to be falsely-high in 10-20% of dogs with normal thyroid function. Some of these dogs have other non-thyroidal illnesses; however, falsely high serum cTSH values have even been reported in clinically normal dogs that had completely normal total T4 and free T4 concentrations.

The high prevalence of false-negative and false-positive test results make this assay unreliable to use as a sole diagnostic test for dogs with suspected hypothyroidism. Further, this assay requires a species-specific reagent as human TSH assays do not work in dogs (or cats). There is no commercial feline TSH assay, and so the cTSH is used.

Hyperthyroid cats predictably have very low cTSH concentrations, whereas high cTSH values have been reported in cats with naturally occurring ypothyroidism, as well as cats with iatrogenic hypothyroidism, i.e., secondary to methimazole or radioiodine-131 treatment.

Normal cats and cats with non-thyroidal illness generally maintain normal cTSH values. Therefore,finding a low total T4 or free T4 in combination with a high cTSH concentration greatly improves the diagnostic sensitivity and precision for identifying hypothyroidism in cats as well as dogs.

## POLYGLANDULAR AUTOIMMUNITY

Individuals genetically susceptible to autoimmune thyroid disease may also become more susceptible to immune-mediated diseases affecting other target tissues and organs, especially the bone marrow, liver, adrenal gland, pancreas, skin, kidney, joints, bowel, and central nervous system. The resulting “polyglandular autoimmune syndrome” of humans is becoming more commonly recognized in the dog, and probably occurs in other species as well. The syndrome tends to run in families and is believed to have an inherited basis. Multiple endocrine glands and nonendocrine systems become involved in a systemic immune-mediated process. This multiple endocrinopathy often occurs in patients with underlying autoimmune thyroid disease (hypo- or hyperthyroidism) and concurrent Addison’s disease, diabetes, reproductive gonadal failure, skin disease and alopecia, and malabsorption syndrome. The most common nonendocrinologic autoimmune disorders associated with this syndrome are autoimmune hemolytic anemia (AIHA), idiopathic thrombocytopenic purpura (ITP), chronic active hepatitis, and immune-complex glomerulonephritis (systemic lupus erythematosus; SLE).

The most commonly recognized polyglandular endocrinopathy of dogs is Schmidt’s syndrome (thyroiditis and Addison’s disease). Examples of breeds genetically predisposed to this disorder include the Standard Poodle, Old English Sheepdog, Bearded Collie, Portuguese Water Dog, Nova Scotia Duck Tolling Retriever, and Leonberger, although any breed or mixed breed can be affected. Our study cohort of 162 cases of autoimmune blood and endocrine disorders in Old English Sheepdogs (1980-1989) included 115 AIHA and/or ITP, 99 thyroid disease, 23 Addison’s disease, 7 vaccine reactions, 3 SLE, 2 diabetes, 1 rheumatoid arthritis and 1 hypoparathyroidism. The group comprised 110 females (15 spayed) and 52 males (3 neutered). Seven of the most recent 103 cases had two or more endocrine disorders, and 101 of the 108 cases where pedigrees were available showed a familial relationship going back several generations. Data from surveying the Bearded Collie breed reported 55 hypothyroid, 17 Addison’s disease, and 31 polyglandular autoimmunity (5 were hypothyroid).

## 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 causes, it also can reflect underlying problems of a psychological nature.

An association between behavioral and psychologic changes and thyroid dysfunction has been recognized in humans since the 19th century. In a recent study, 66% of people with attention deficit-hyperactivity disorder were found to be hypothyroid, and supplementing their thyroid levels was largely curative. Furthermore, an association has recently been established between aberrant behavior and thyroid dysfunction in the dog, and has been noticed in cats with hyperthyroidism. 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 mechanism whereby diminished thyroid function affects behavior is unclear. Hypothyroid patients have reduced cortisol clearance, as well as suppressed TSH output and lowered production of thyroid hormones. Constantly elevated levels of circulating cortisol mimic the condition of an animal in a constant state of stress. In people and seemingly in dogs, mental function is impaired and the animal is likely to respond to stress in a stereotypical rather than reasoned fashion. Chronic stress in humans has been implicated in the pathogenesis of affective disorders such as depression. Major depression has been shown in imaging studies to produce changes in neural activity or volume in areas of the brain which regulate aggressive and other behaviors. Dopamine and serotonin receptors have been clearly demonstrated to be involved in aggressive pathways in the CNS. Hypothyroid rats have increased turnover of serotonin and dopamine receptors, and increased sensitivity to ambient neurotransmitter levels.

Investigators in recent years have noted the sudden onset of behavioral changes in dogs around the time of puberty or as young adults. Most of the dogs have been purebreds or crossbreeds, with an apparent predilection for certain breeds. For a significant proportion of these animals, neutering does not alter the symptoms and in some cases the behaviors intensify. The seasonal effects of allergies to inhalants and ectoparasites such as fleas and ticks, followed by the onset of skin and coat disorders including pyoderma, allergic dermatitis, alopecia, and intense itching, have also been linked to changes in behavior.

Many of these dogs belong to a certain group of breeds or dog families susceptible to a variety of immune problems and allergies (e.g. Golden Retriever, Akita, Rottweiler, Doberman Pinscher, English Springer Spaniel, Shetland Sheepdog, and German Shepherd Dog). The clinical signs in these animals, before they show the sudden onset of behavioral aggression, can include minor problems such as inattentiveness, fearfulness, seasonal allergies, skin and coat disorders, and intense itching. These may be early subtle signs of thyroid dysfunction, with no other typical signs of thyroid disease being manifested.

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. This can progress to sudden unprovoked aggressiveness in unfamiliar situations with 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. Two recent cases involved young dogs referred for sudden onset seizure disorder shortly after puberty. Both dogs were found to have early onset autoimmune thyroiditis, which was clinically responsive to thyroid supplementation, to the extent that anticonvulsant medications could be gradually withdrawn. The numbers of animals showing various types of aberrant behavior are increasing in frequency over the last decade.

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.

Results of complete thyroid diagnostic profiling were analyzed on the first 634 canine cases of aberrant behavior, compiled by this author in collaboration with Drs. Nicholas Dodman, Linda Aronson, and Jean DeNapoli of Tufts University School of Veterinary Medicine, North Grafton, MA. Ninety percent (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 3 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 4 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 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.

## MANAGEMENT & THERAPY

### Dogs

Remember that thyroxine binds to calcium and soy and so this drug should be given apart from meals (1 hr before or 3 hrs after), regardless of what the product label says. While physicians are taught about the binding behavior of this drug to alert their patients, veterinarians traditionally have never been told about it.

Dogs testing positive for heritable autoimmune thyroiditis should be treated with thyroxine twice daily immediately, even if their basal thyroid levels are still normal (i.e. in “compensative autoimmune thyroiditis”).This is because feedback inhibition of TSH output from the pituitary gland shuts off stimulation of thyroid gland receptors, and stops thyroid autoantibody production. It typically takes ~ 5-7 months or longer of therapy, but thyroid autoantibody levels should gradually decline until they are normal (negative). However, therapy with thyroxine is needed lifelong to prevent the reoccurrence of autoantibody production.

Because of the heritable nature of this trait, as discussed above, dogs affected with thyroiditis, even if still asymptomatic should *not* be used for breeding purposes.

### Cats

Hyperthyroid cats after diagnosis are typically treated with oral (tablet or compounded liquid) or transdermal ear tip application of methimazole, radioactive iodine-131 therapy to ablate the thyroid acinar cells, or surgical removal of the thyroid adenoma(s).

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## Table 1. Clinical Signs of Canine Hypothyroidism

| | |
|---|---|
| **Alterations in Cellular Metabolism** | |
| lethargy | weight gain or weight loss |
| mental dullness | cold intolerance |
| exercise intolerance | mood swings |
| neurologic signs | hyperexcitability |
| polyneuropathy | stunted growth |
| seizures | chronic infections |
| **Neuromuscular Problems** | |
| weakness | knuckling or dragging feet |
| stiffness | muscle wasting |
| laryngeal paralysis | megaesophagus |
| facial paralysis | head tilt |
| "tragic" expression | drooping eyelids |
| incontinence | ruptured cruciate ligament |
| **Dermatologic Diseases** | |
| dry, scaly skin and dandruff | chronic offensive skin odor |
| coarse, dull coat | bilaterally symmetrical hair loss |
| "rat tail"; "puppy coat" | seborrhea with greasy skin |
| hyperpigmentation | seborrhea with dry skin |
| pyoderma or skin infections | myxedema |
| **Reproductive Disorders** | |
| infertility | prolonged interestrus interval |

| | |
|---|---|
| lack of libido | absence of heat cycles |
| testicular atrophy | silent heats |
| hypospermia | pseudopregnancy |
| aspermia | weak, dying or stillborn pups |

**Cardiac Abnormalities**

| | |
|---|---|
| slow heart rate (bradycardia) | cardiac arrhythmias |
| cardiomyopathy | |

**Gastrointestinal Disorders**

| | |
|---|---|
| constipation | inappetance or picky eater |
| diarrhea | vomiting |
| inflammatory bowel disease | flatulence |

**Hematologic Disorders**

bleeding
bone marrow failure
low red blood cells (anemia), white blood cells, platelets

**Ocular Diseases**

| | |
|---|---|
| corneal lipid deposits | corneal ulceration |
| uveitis | keratoconjunctivitis sicca or "dry eye" |
| infections of eyelid glands (Meibomian gland) | Vogt-Koyanagi-Harada syndrome |

**Other Associated Disorders**

| | |
|---|---|
| IgA deficiency | loss of smell (dysosmia) |
| loss of taste | glycosuria |
| other endocrinopathies<br>adrenal<br>pancreatic<br>parathyroid | chronic or reactive hepatitis |

### Table 2. Diagnosis of Thyroid Disease

- Complete Basic Thyroid 5 Profile
  -- T4, T3, FT4, FT3, TgAA
- Additional Tests
  -- T3AA, T4AA ,TgAA; cTSH (optional)

- **Older Tests (T4, T4 + T3)**
  Serum T4 and/or T3 alone are **not** reliable for diagnosis because:
  -- overdiagnose hypothyroidism
  -- underdiagnose hyperthyroidism
  -- fail to dectect early compensatory disease and thyroiditis
  -- influenced by nonthyroidal illness and certain drugs
- **Newer Tests**
  **Free (Unbound) T4**
  Less likely to be influenced by nonthyroidal illness or drugs
  Valid -- equilibrium dialysis
  -- solid-phase analog RIA

-- chemiluminescence solid-phase
Less reliable -- liquid-phase analog RIA

**T4/FT4 Ratio (dogs only)**
Accurately distinguishes thyroid dysfunction from non-thyroidal illness (NTI)
-- results from 1000 healthy dogs during a 6-week period revealed a tight T4:FT4 ratio ranging from 1.30-1.54
-- Ratios below 1.25 indicate the presence of primary or secondary NTI
--variance of data for dogs with liver disease *not* receiving thyroxine much higher than that of dogs with high ALT taking thyroxine (2.225 vs 0.085)

**Endogenous Canine TSH**
In primary hypothyroidism, as free T4 levels fall, pituitary output of TSH rises
-- elevated TSH usually indicates primary thyroid disease
-- reulatory control in dogs also by growth hormone, unlike people
-- 30% discordancy observed between expected and actual findings
-- published normal ranges may need revising
-- affected by concomitant chronic renal disease
-- helpful in hyperthyroid cats post-I-131 to monitor thyroid status

**Canine TgAA**
Thyroglobulin autoantibodies present in serum of lymphocytic thyroiditis cases
-- positive results confirm diagnosis ; 8% false negative
-- 20-40% of cases have circulating T3 and/or T4AA
-- allows for early diagnosis and genetic counseling