Update: Thyroid disorders

Pathogenesis of hyperthyroidism

Feline hyperthyroidism was first described in 1979 and 1980 by investigators in NYC and Boston. During a 14 year period from 1970-1984, an average of 1.9 cats per year were diagnosed with hyperthyroidism; however, it is now estimated that the incidence is as high as 2% of the feline population seen in tertiary care veterinary facilities. Since then, hyperthyroidism has become the most frequently diagnosed endocrinopathy in the cat with reports stemming from North America, Europe (esp UK), New Zealand and Australia.

Canned cat food has been implicated as a cause of feline hyperthyroidism in multiple epidemiological studies. (Kass 1999, Martin 2000, Edinboro 2004) The suspected goitrogen is bisphenol-A-diglycidyl ether (BADGE), a substance used in making the liner of easy-open “pop-top” cans. It is suspected that this compound can leach into the foods and be consumed by cats. While this BADGE-based lining is generally considered safe and is used for foods for human consumption, cats may be more susceptible to toxic effects of this compound because they have a greatly reduced ability to detoxify it via hepatic glucuronidation. Bisphenol A also reduces triiodothyronine binding and causes increased TSH secretion resulting in hyperthyroidism and goiter in rats and some humans. While cat studies may not be available, rodent studies show a very high safety margin. (Poole 2004) It should be noted that epidemiological studies showing associations are not the same as cause and effect. Over 90% of cats in the US consume commercial pet foods as their primary nutritional source, and relatively few develop hyperthyroidism.

More recently, investigators have honed in on the molecular aspects of feline hyperthyroidism. The disease in cats is more similar to toxic nodular goiter in humans and is characterized by autonomous growth of thyroid follicles. The pathogenesis of toxic nodular goiter is an abnormality in the signal transduction of the thyroid cell. The TSH receptor on the thyroid cells activated receptor-coupled guanosine triphosphate-binding proteins (G proteins). Uniquely, the thyroid cell proliferation and hormone production are both controlled by the TSH receptor- G-protein-cAMP signaling. Overexpression of stimulatory G proteins and underexpression of inhibitory G proteins have been demonstrated in some humans with toxic nodular goiter. (Derwalht 1995, Delmer 1992) Mutations of the TSH receptor that result in the receptor remaining activated without ligand (ie, TSH) have also been reported in humans with toxic nodular goiter. (Parma 1997, Fuhrer 1997, Holzapfel 1997, Russo 1996) In hyperthyroid cats, the same abnormalities have been investigated and it appears that activation mutation of the TSH receptor may be part of the pathogenesis of feline hyperthyroidism in some cats. (Peeters 2002) Furthermore, abnormalities of G proteins, specifically significantly decreased G inhibitory protein expression has been described in tissues from hyperthyroid cats. (Hammer 2000)
In one study, the use of cat litter was associated with an increased risk of hyperthyroidism (Kass 1999); however, there was no significant difference between different litter brands suggesting that the use of litter is simply a marker of cats that are kept indoors. (Peterson and Ward 2007) Indoor cats are likely to live longer and hence have a higher risk of developing hyperthyroidism. Exposure to pesticides and herbicides has been associated with thyroid abnormalities in other species. (Gaitan 1990) In particular, the use of flea control products was associated with an increased risk of developing hyperthyroidism; however, no specific product or ingredient could be identified. (Scarlett 1988, Olkzak 2005)

One recent report implicated brominated flame retardants (BFRs) as carcinogens/goitrogens possibly associated with feline hyperthyroidism. (Dye 20007) Coincidently BFRs were introduced 30 years ago at the same time that feline hyperthyroidism emerged. Bromide, a halide, is an intriguing agent to implicate in feline hyperthyroidism because of the unique composition of thyroid hormones which contain the halide iodide. In this recent abstract, serum levels of lipid adjusted serum polybrominated diphenylethers (PBDE) levels were 10-400-fold higher than those found in human exposure. The authors theorized that these findings of high PBDE serum levels is in accord with the most consistently identified risk factor which is “indoor living”. The authors also propose that cats are at increased risk because of meticulous grooming behavior and increased exposure to furniture and carpets. The small size of cats is also a possible risk factor for increased serum levels of PBDEs. Recent publications point to PBDEs as the most likely environmental contaminant that may contribute to feline hyperthyroidism. (Peterson 2012)

**Medical Therapy**

Medical management requires no special facilities and is readily available. Anesthesia is avoided, as are the surgical complications associated with thyroidectomy. However, this form of treatment is not curative and requires regular biochemical monitoring to ensure the efficacy of treatment. The thyroid tumor continues to grow and, after many months, may transform from adenoma to thyroid carcinoma in approximately 10% of chronically treated cats. (Peterson 2012)

Long-term medical management best reserved for cats of advanced age or for those with concurrent diseases, and for when owners refuse either surgery or radioactive iodine. In addition to long-term treatment, medical management is also necessary prior to surgical thyroidectomy to decrease the metabolic and cardiac complications associated with hyperthyroidism.

Short-term medical management is often recommended as trial therapy prior to 131-I therapy to determine the effect of restoring euthyroidism on renal function.
Methimazole is specifically licensed for treatment of feline hyperthyroidism both in Europe and USA as 2.5-mg and 5-mg tablets (Felimazole, Dechra Veterinary Products). For most hyperthyroid cats, a starting dose of 1.25 to 2.5 mg methimazole administered once to twice daily is recommended. Methimazole can be reformulated in an organogel for transdermal administration and is effective in cats when administered at a dose of 2.5 mg twice daily transdermally. The gel is applied in a thin layer to the non-haired portion of the pinnae. Transdermal administration is associated with fewer gastrointestinal side effects than the oral route, but some cats resent manipulation of their ears and crusting can occur between doses leading to erythema.

Monitoring of cats on antithyroid drugs is extremely important. Initially, cats should be reassessed after 2 to 3 weeks and a serum total T4 concentration measured. If euthyroidism has not been achieved the dose of methimazole or carbimazole can be altered in 2.5 to 5-mg increments, reassessing the cat again in 2 to 3 weeks. Lack of owner or cat compliance should first be eliminated as a reason for a failure of therapy. When monitoring, time of serum T4 sampling in relation to the administration of the antithyroid drug is not important. The goal of medical therapy is to maintain total T4 concentrations within the middle third of the reference range.

Once the dosage has stabilized, the cat should be monitored every 3 to 6 months and as needed clinically. Because antithyroid medications have no effect on the underlying lesion, the thyroid nodules continue to grow larger and larger over time. This may necessitate an increased daily dose with time.

Most clinical adverse reactions occur within the first 3 months of therapy. Mild clinical side effects of vomiting, anorexia, or depression occur in approximately 10-15% of cats, usually within the first 3 weeks of therapy. Mild and transient hematological abnormalities, including lymphocytosis, eosinophilia or leucopenia, develop in up to 15% of cats without any apparent clinical effect. More serious hematological complications occur in less than 5% of cats and include agranulocytosis and thrombocytopenia.

Self trauma in the form of excoriations of the head and neck occasionally develop, usually within the first 6 weeks of therapy. Hepatopathy characterized by marked increases in liver enzymes and bilirubin concentration occurs in less than 2% of cats. Withdrawal of the medication and symptomatic therapy is required. Other rarely reported side effects include a bleeding tendency without thrombocytopenia, prolongation of clotting times, and acquired myasthenia gravis.

**Nutritional therapy (Hill y/d)**

This is an iodine-deficient diet, containing levels below the minimum daily requirement for adult cats. By 12 weeks, almost all cats should have normal T4 values.
This therapy appears to be more effective in cats with only moderate elevations of T4 than cats with severe hyperthyroidism.

A major indication for the use of this y/d diet for management of feline hyperthyroidism is in cats that are not candidates for definitive treatment of the underlying thyroid tumor(s) with surgery or radioiodine, which remains the treatments of choice. Nutritional management with y/d food (canned rather than the dry y/d) could be considered in cats whose owners are not able to give oral medication or in cats that develop side effects from methimazole/carbimazole.

The thyroid tumor remains and will continue to grow larger. In cats with long-standing hyperthyroidism, transformation of adenoma to thyroid carcinoma can occur unless definitive treatment (surgery or radioiodine treatment) is used to cure the disease. The cats fed this diet must not eat any other cat diet, table food, or treats because even tiny amounts of iodine may lead to failure of this diet to effectively control hyperthyroidism. The composition (protein/fat/carbohydrate breakdown) of y/d reveals that it is a high-carbohydrate, relatively low-protein diet. Feeding y/d for long periods is less than an “ideal” diet for an obligate carnivore, especially in an older hyperthyroid cat with severe muscle wasting (Table 1).

Surgical therapy

Surgical therapy entails either unilateral or bilateral thyroidectomy. Because most cats have involvement of both thyroid lobes, bilateral thyroidectomy is indicated in most cats. The two major techniques for bilateral thyroidectomy include the intracapsular and extracapsular methods. The aim of both techniques is to remove the adenomatous thyroid tissue while preserving parathyroid function. The major problem with the intracapsular technique for thyroidectomy is that it can be difficult to remove the entire thyroid capsule (and, therefore, all abnormal thyroid tissue) while concurrently preserving parathyroid function.

The most serious complication is hypocalcemia, which develops after the parathyroid glands are injured or inadvertently removed. Since only one parathyroid gland is required for maintenance of normocalcemia, hypoparathyroidism develops only in cats treated with bilateral thyroidectomy. After bilateral thyroidectomy, it is important to monitor serum calcium concentration daily until it has stabilized within the normal range. In most cats with iatrogenic hypoparathyroidism, clinical signs associated with hypocalcemia will develop within 2 to 5 days of surgery. Temporary hypothyroidism develops in most cats after unilateral or bilateral thyroidectomy, with serum T4 concentrations falling to subnormal levels for 2 to 3 months. However, clinical signs of hypothyroidism are rare. Because of the potential for recurrence of hyperthyroidism, all cats should have serum T4 concentration monitored once or twice a year (Table 1).
Radioactive iodine therapy

I-131 treatment avoids inconvenience of daily oral administration of antithyroid drugs as well as the side effects commonly associated with these drugs. Eliminates the risks and perioperative complications associated with anesthesia and surgical thyroidectomy. Its use requires special radioactive licensing and hospitalization facilities, and extensive compliance with local and state radiation safety laws.

Major drawback for most owners is that their cat must be kept hospitalized for a period (3 to 10 days in most treatment centers; but up to a month in some places) and visiting is not allowed. More precision can be gained with thyroid imaging (scintigraphy) since it can also be used to estimate thyroid tumor volume and identify ectopic (intrathoracic) thyroid tissue.

A proportion of cats treated with radioiodine will develop permanent hypothyroidism, with clinical signs developing 3 to 6 months after treatment. Clinical signs associated with iatrogenic hypothyroidism are generally very mild but may include lethargy, non-pruritic seborrhea sicca, matting of hair, and marked weight gain; bilateral symmetric alopecia does not develop. Diagnosis of hypothyroidism is based upon clinical signs, subnormal serum total T4 and free T4 concentrations, high serum cTSH values, and the response to replacement L-T4 therapy). Life-long L-T4 supplementation is needed (i.e., 0.1-0.2 mg L-thyroxine per day).

In cats with thyroid carcinoma (incidence <2-4% of all hyperthyroid cats), radioiodine offers the best chance for successful cure of the tumor because it concentrates in all hyperactive thyroid cells, i.e., carcinomatous tissue, as well as metastasis.

V References


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Association of Iatrogenic Hypothyroidism with Azotemia and Reduced Survival Time in Cats Treated for Hyperthyroidism

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Background: Iatrogenic hypothyroidism can occur after treatment of hyperthyroidism, and is correlated with a reduced glomerular filtration rate in humans and dogs.

Hypothesis: Cats with iatrogenic hypothyroidism after treatment for hyperthyroidism will have a greater incidence of azotemia than euthyroid cats.

Animals: Eighty client owned cats with hyperthyroidism.

Methods: Two retrospective studies. (1) Longitudinal study of 12 hyperthyroid cats treated with radioiodine (documented as euthyroid after treatment), to assess changes in plasma thyroid stimulating hormone (TSH) concentration over a 6-month follow-up period, (2) Cross-sectional study of 75 hyperthyroid cats (documented as euthyroid) 6 months after commencement of treatment for hyperthyroidism to identify the relationship between thyroid status and the development of azotemia. Kaplan-Meier survival analysis was performed to identify relationships between thyroid and renal status and survival.

Results: Plasma TSH concentrations were not suppressed in 7 of 8 cats with hypothyroidism 3 months after radioiodine treatment. The proportion of cats with azotemia was significantly (P = .028) greater in the hypothyroid (16 of 28) than the euthyroid group (14 of 47). Twenty-eight of 41 cats (68%) with plasma TT4 concentration below the laboratory reference range had an increased plasma TSH concentration. Hypothyroid cats that developed azotemia within the follow-up period had significantly (P = .018) shorter survival times (median survival time 456 days, range 231–1589 days) than those that remained nonazotemic (median survival time 905 days, range 316–1869 days).

Conclusions and Clinical Importance: Iatrogenic hypothyroidism appears to contribute to the development of azotemia after treatment of hyperthyroidism, and reduced survival time in azotemic cats.

Key words: Euthyroid-sick syndrome; Subclinical hypothyroidism; Thyroid stimulating hormone.

Canine Hypothyroidism

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Hypothyroidism is the most common and frequently diagnosed endocrinopathy of the dog.\(^1,2\) It is a rare phenomenon in cats.\(^1\) The thyroid, under the influence of thyrotropin (TSH), produces the hormones thyroxine (T4) and 3,5,3’-triiodothyronine (T3). Thyroxine and T3 have many affects on cellular metabolism and their levels in the body are tightly regulated. Dysregulation of T3 and T4 levels has far reaching effects. The signs of thyroid hormone deficiency are vague, non-specific and not pathognomonic. No single test exists with which to make a definitive diagnosis. Instead, a diagnosis of hypothyroidism is made based on a combination of clinical signs, physical examination findings, biochemical abnormalities and thyroid function tests. With a combination of tests, a diagnosis of hypothyroidism can be reached with confidence. However, clinicians must keep in mind that non-thyroidal illness, some medications, physical activity level and antithyroglobulin antibodies, alter results of thyroid function tests. Once a diagnosis has been made this disease can be easily controlled with thyroid hormone supplementation. A rare but serious complication of severe hypothyroidism is myxedema coma.

**Physiology**

Iodine and tyrosine are the basic substrates involved in thyroid hormone synthesis. Dietary iodide is actively transported into thyroid follicular cells and oxidized to iodine by thyroperoxidase. Iodine then binds to tyrosine residues on thyroglobulin to form monoiodotyrosine (MIT) and diiodotyrosine (DIT). Coupling of MIT and DIT forms both T3 (MIT-DIT) and T4 (DIT-DIT), which are bound to thyroglobulin and stored in the colloid. Under the control of TSH, thyroglobulin undergoes proteolysis in phagolysosomes, releasing T3 and T4.\(^3,4\) Thyroid hormones are water-insoluble and their ability to circulate is dependent on binding to thyroxine-binding globulin, thyroxine-binding prealbumin or albumin. Most thyroid hormone (>99%) is protein bound with the remaining unbound portion being the metabolically active or “free” form.\(^3,5\) These binding proteins are reservoirs for circulating thyroid hormone and allow for the free hormone level to be maintained within a very narrow range. T4 is the main secretory product of the thyroid. However, T3 is more biologically active and is most effective in binding to and activating the thyroid hormone nuclear receptor. Once in peripheral tissues, T4 is deiodinated to T3 prior to receptor binding. The majority of T3 (40% to 60%) is derived from extrathyroidal deiodination of T4.\(^3,4\) The production and release of thyroid hormones is controlled by a classic negative feedback mechanism (Figure 1). The hypothalamic-pituitary-thyroid axis is responsible for maintaining control of extrathyroidal hormone levels. The hypothalamus produces thyrotropin releasing hormone (TRH), which stimulates thyrotropes in the anterior pituitary to produce TSH. In addition to hormone release, TSH stimulates growth of the thyroid gland.\(^4\) Thyroid hormones, particularly T3, provide the feedback to the hypothalamus and pituitary to down regulate TRH and TSH production.

**Pathophysiology**

Hypothyroidism can be classified as acquired or congenital. Acquired hypothyroidism can be primary, secondary or tertiary and is usually a disease of adult dogs with the average age at diagnosis being 7 years.\(^2\) Primary hypothyroidism is associated with destruction of the tissue of the thyroid and the thyroid becomes less responsive to TSH. Therefore T3 and T4 levels gradually decline, with a compensatory increase in TSH.
There are two common histologic forms of primary hypothyroidism. The first is lymphocytic thyroiditis, thought to be an immune mediated process, which eventually results in thyroid atrophy. The second, idiopathic thyroid atrophy, is a separate form of thyroid destruction which does not demonstrate an inflammatory component; however, it may be the end stage of lymphocytic thyroiditis. Together these processes account for 95% of the clinical cases of hypothyroidism in dogs. This is comparable to people where 99% of hypothyroidism is the result of these mechanisms. Lymphocytic thyroiditis is characterized by chronic and progressive lymphocytic infiltration and destruction of the thyroid gland. Cytotoxic T-cells set up inflammation leading to thyrocyte destruction and parenchymal fibrosis. This process is gradual and accounts for the slow onset of clinical signs associated with hypothyroidism. The immune mediated process is associated with the production of autoantibodies, predominantly against thyroglobulin. However, autoantibodies against T3 and T4 have been reported. While T3 and T4 are haptens, they are attached to thyroglobulin, which appears to act as the antigenic stimulus for the production of antibodies. This differs from people where the immune target is thyroperoxidase. Recent vaccination may cause an elevation in antithyroglobulin antibodies not associated with primary hypothyroidism. Autoantibodies cross react with T4 assays. This fact is of clinical importance because in situations where autoantibodies are present, the total serum T4 can be elevated into the reference or hyperthyroid ranges, causing the clinician to miss the diagnosis of hypothyroidism. Rare causes of primary hypothyroidism include neoplastic destruction of thyroid tissue, iodine deficiency, infection and iatrogenic destruction secondary to drugs, surgery or radiiodine treatment.

Secondary and tertiary hypothyroidism are rare. With secondary hypothyroidism the defect is localized to the pituitary and there is an impaired ability to synthesize and secrete TSH. Secondary hypothyroidism may be caused by pituitary tumors, congenital malformation of the pituitary, infection or by TSH suppression. TSH suppression can be caused by drugs, hormones or concurrent illness. Tertiary hypothyroidism is hypothalamic in origin and production of TRH is either decreased or nonexistent. Tertiary hypothyroidism has not been reported in the veterinary literature. Both secondary and tertiary hypothyroid patients would be expected to demonstrate an increase in thyroid hormone levels in response to TSH or TRH stimulation respectively.

Congenital hypothyroidism, rarely seen in veterinary medicine, is caused by inherited defects or by exposure of the fetus or newborn to either an excess or deficiency of dietary iodine. Congenital hypothyroidism is categorized as goitrous or non-goitrous. Goiter, the term for enlargement of the thyroid gland, develops when there is increased release of TSH along with an intact thyroid TSH receptor. Clinical signs of congenital hypothyroidism include developmental delays, both mental and physical, and dwarfism. An autosomal recessive form of congenital hypothyroidism has been reported in Toy Fox Terriers, Giant Schnauzers and Abyssinian cats. Affected animals have a thyroid peroxidase deficiency. Genetic testing is available to detect carrier Fox Terriers. Congenital hypothyroidism is also noted as an element of panhypopituitarism.

Clinical Signs and Routine Blood Analysis
Clinical signs associated with hypothyroidism are vague and involve many different systems. The most commonly reported clinical signs include dermatologic abnormalities, weight gain, lethargy, and weakness. Most changes appear to be secondary
to decreased metabolism due to the lack of circulating thyroid hormones.

Dermatologic changes, including alopecia, seborrhea and pyoderma are commonly associated with hypothyroidism. However, changes in the epidermis and hair coat are often breed specific\(^{24,25}\) and are not noted in every patient. The value of skin biopsies is controversial\(^1\) as many cutaneous changes are nonspecific and biopsies from different endocrinopathies may demonstrate similar changes.\(^{26}\) However, certain findings, including dermal thickening, myxedema and vacuolation of arrector pili muscles, are most characteristic of hypothyroidism.\(^{24}\) Bilateral symmetric nonpruritic truncal alopecia is reported in 88% of hypothyroid dogs.\(^{23}\) Thyroid hormones are required for the initiation of anagen (active hair growth). In hypothyroid animals most hair follicles are retained in telogen (the quiescent or resting phase of the hair cycle). Without thyroid hormones, the hair coat becomes dry, dull and brittle. Hair loss is noted in areas of increased wear and usually includes the ventral thorax and neck, ventral abdomen and tail. Loss of primary hair is most common with guard hairs being retained, resulting in a short fine hair coat.\(^{19,23}\) Hyperpigmentation may be noted in areas of alopecia.

Other skin changes include dry, scaly skin, pyoderma, dermatitis, seborrhea, hyperkeratosis, myxedema and otitis externa. Thyroid hormone enhances the lymphoid immune response.\(^{26}\) In the hypothyroid state, there is a decrease in T-cell function and humoral immunity.\(^1\) This decrease in local immunity causes the skin to become more susceptible to infection. Pyoderma has been reported in 14% of dogs with hypothyroidism.\(^{23}\) Generalized demodicosis and *Malassezia* spp infections are common.\(^{24}\) An increased incidence of otitis externa also tends to be noted compared to non-hypothyroid dogs. Primary dermatologic conditions such as alopecia, dry skin and seborrhea are non-pruritic, but pruritis will often accompany secondary parasitic, yeast or bacterial infections.\(^1,24\)

Neurologic abnormalities are rare. Most neurologic signs are associated with polyneuropathy and include weakness, facial nerve paralysis, vestibular signs (usually peripheral) and hyporeflexia. Segmental demyelination and axonopathy are a likely pathogenesis of these clinical signs; however, myxedema causing compression of the VII and VIII cranial nerves may be another pathogenesis of the facial and vestibular nerve dysfunction.\(^{27,28}\) Megaeosophagus and laryngeal paralysis have both been suggested to be associated with hypothyroidism; however, there are no data to support this association.\(^{23,29}\) A causal relationship between hypothyroidism and myasthenia gravis remains to be proven.\(^{30,31}\) Central nervous system signs, including seizures, ataxia, behavior changes and coma, are rarely seen. They may result from myxedema, lack of thyroid hormone, hyponatremia or decreased blood flow to the brain.\(^{1,32,33}\)

Several reproductive abnormalities have been suggested to be associated with hypothyroidism. For males these include decreased fertility, testicular atrophy, poor semen motility and decreased libido.\(^1\) In females, hypothyroidism has been suggested to be associated with prolonged interestrus periods, failure to cycle, decreased libido and inappropriate mammary gland development.\(^1\) There have been no data to support any association between decreased thyroid hormone levels and reproductive failure in either males or females.\(^{34,35}\) When reproductive failure is detected, causes besides hypothyroidism must also be investigated.

Cardiovascular abnormalities though rare have been reported. Cardiovascular signs may be
secondary to problems with conduction or direct myocardial effects. Bradycardia, arrhythmias, decreased conduction, decreased contractility and diastolic dysfunction have all been reported. In the hypothyroid state there is a decreased B-adrenergic receptor number, accounting for decreased contractility and lower heart rates. Congestive heart failure has not been documented secondary to hypothyroidism in dogs, which is in contrast to people.

Ocular changes can include corneal cholesterol deposits, keratoconjunctivitis sicca and conjunctivitis, though these signs are reported in less than 1% of all hypothyroid dogs.

On serum biochemistry, hypercholesterolemia, hypertriglyceridemia and hyponatremia are commonly noted. These changes are the result of the decrease in normal lipid metabolism accompanying hypothyroidism. Hypothyroid dogs have increased very low density lipoproteins, low density lipoproteins and high density lipoproteins. Increased triglyceride levels may play a role in the development of pancreatitis, though this association has not been proven. Elevated levels of cholesterol and triglycerides have been associated with atherosclerosis in dogs, though this is rare.

Anemia is another common finding. Twenty-eight to 32% of hypothyroid dogs demonstrate anemia. The anemia is usually normochromic, normocytic and non-regenerative and likely results from one of or a combination of three mechanisms. There may be decreased erythropoietin production, a reduced response of progenitor cells to erythropoietin or decreased stimulation of early hematopoietic stem cells. The hypothyroid state does not affect red blood cell life span.

**Thyroid Function Tests**

Quantitative technium scans and thyroid biopsy are considered the gold standard for the diagnosis of hypothyroidism. However, as noted below, there is limited access to test reagents and the cost is often prohibitive. Other tests are available to help clinicians evaluate thyroid function, thyroid hormone levels and antithyroglobulin antibody levels. These tests include total T4 (TT4), endogenous canine TSH (cTSH), free T4 (fT4-ED or CLIA), antithyroglobulin antibodies (ATA), anti-T3 antibodies, anti-T4 antibodies, total T3 (TT3), free T3 (fT3) and reverse T3 (rT3).

A commonly requested initial test to screen thyroid function is TT4. Total T4 measures both the protein bound T4 and the fT4. Total T4 is a direct assessment of the functional ability of the thyroid tissue to produce hormone. A decreased TT4 is a common finding in a hypothyroid animal making this a very sensitive test; however, it is not diagnostic of hypothyroidism and necessitates further more specific testing in order to confirm the diagnosis. TT4 can be measured by enzyme-linked immunosorbent assay (ELISA), by chemiluminescence or by radioimmunoassay (RIA).

Measurement of endogenous TSH is available using a canine assay. Because of cross reactivity, this assay may also be used for cats. In the hypothyroid state, the TSH level would be expected to be elevated, due to loss of negative feedback. Evaluation of TSH is a test with a high specificity and low sensitivity. Since TT4/fT4 and TSH are both elements of the feedback mechanism of the hypothalamic-pituitary-thyroid axis, they should be
interpreted together. In other words to accurately understand the significance of a TSH level, the clinician should know the TT4 or fT4 level. Current methods for assessing TSH levels are not sensitive at low levels. Therefore TSH cannot be used to make a diagnosis of secondary hypothyroidism. Finally, because an animal does not become hypothyroid overnight, a diagnosis of early hypothyroidism may require multiple serial measurements of eTSH and TT4. A rising eTSH is very suggestive of ongoing thyroid destruction associated with immune mediated primary hypothyroidism.

Free T4 measures the metabolically active portion of TT4. This fraction of the hormone is able to enter the cell, be converted into T3 and interact with the thyroid hormone receptor. Hypothyroid animals would be expected to have a low fT4. This test, like TT4, has most value as a screening test. Concurrent illness has less effect on fT4 levels, compared to TT4.43,46 However, glucocorticoids, phenobarbital and hyperadrenocorticism have been noted to cause a decreased fT4.47-49 There are different methods by which to measure serum fT4. Measurement by equilibrium dialysis has been demonstrated to be reliable when compared to RIA.50 Chemiluminescent assays for free T4 have been shown to have a sensitivity of 88% and a specificity of 96% in hypothyroid dogs. (Table 1). Recently, a veterinary specific chemiluminescent immunoassay for free T4 was shown in a multicenter clinical evaluation to have a comparable diagnostic accuracy as the free T4 ED test. (abstract and IDEXX white paper??) Lastly, some authorities believe (and unpublished results suggest) that the currently used free T4 ED assays do not perform as well as the free T4 ED assay (made by Nichols Diagnostics) that was used to assess the free T4 ED assay in the published studies in dogs and cats. (Peterson, ACVIM Advanced Endo Course, 2010).

Immune mediated thyroiditis may result in the production of antithyroglobulin, anti-T3 or anti-T4 antibodies. It is possible to test for ATA and a positive titer is predictive of immune mediated thyroiditis19,10 and suggestive of hypothyroidism.51 The anti-T3 and T4 antibodies may create a problem when attempting to make a diagnosis of hypothyroidism. The antibodies are similar to T3 and T4 and will cross react to falsely elevate assay levels.10,15 Therefore if anti-T4 antibodies are present, the TT4 level will be reported to be higher than it actually is. This situation is of most concern for animals whose TT4 is truly just below the normal range. With the presence of anti-T4 antibodies, these animals may actually appear to be euthyroid, thus delaying diagnosis and treatment of hypothyroidism. Free T4 measured by dialysis is not affected by the presence of antithyroglobulin, anti-T3 or anti-T4 antibodies.15 In some situations the ATA will be positive but the TT4 and fT4 levels will be well within normal ranges and the animal will not be exhibiting any clinical signs associated with hypothyroidism. These cases demand close monitoring and re-evaluation, as these may be animals at risk of developing hypothyroidism.

For many years the TSH stimulation test was used to diagnose hypothyroidism52,53 This test was routinely run using pharmaceutical grade bovine TSH. With the introduction of recombinant human TSH (rhTSH) production of pharmaceutical grade bovine TSH halted. Recent studies have been published demonstrating that rhTSH can be used in both dogs and cats safely and effectively in order to perform a TSH stimulation test.54,55 Adverse side effects of rhTSH in people include headache and nausea, no side effects of any sort were reported in cats or dogs. Recombinant human TSH is very expensive and while its’ use is validated, it is unlikely to become routine and displace TT4, fT4 and TSH as the diagnostic.
tests of choice.

Serum TT3 measurement is an unreliable indicator of thyroid function. The TT3 has been demonstrated to be normal in up to 90% of all hypothyroid dogs.46 Reverse T3 has not been validated in companion animals with case controlled studies. Therefore evaluation of TT3, fT3 and rT3 is not routinely recommended for assessment of thyroid function in dogs.1,43

Recently, another tool has become available to assist in the diagnosis of hypothyroidism. Two reports have indicated ultrasound of the thyroid gland is helpful in distinguishing between hypothyroid and euthyroid dogs. The studies demonstrated significant differences in thyroid gland volume and echogenicity between hypothyroid and euthyroid patients. There was no significant difference between euthyroid and sick euthyroid subjects. These studies conclude ultrasonography can be an adjunctive diagnostic tool to assist in the diagnosis of canine hypothyroidism.56,57 Limitations of this test include the need for high quality ultrasonography equipment and a skilled and trained operator to complete the test. In the future this test may become more widespread and routine.

All available tests are tools veterinarians can use to help arrive at the diagnosis of hypothyroidism. Investigation of hypothyroidism should be based on an increased index of suspicion. Assessment of a CBC, serum biochemistry and urine analysis is helpful for ruling out the presence of nonthyroidal illness (Figure Two). The next step would be to run a highly sensitive test (TT4) for screening and a more specific test (cTSH) to help confirm a diagnosis (Table Three). There may be some instances when a concurrent illness is not able to be resolved (i.e. diabetes mellitus, chronic renal failure), since TSH is minimally affected by concurrent disease, it is still recommended to proceed with these tests. The data from Table Three demonstrate that by using a combination of tests the clinician is able to arrive at a highly reliable result. There will however be situations where the results of the tests are unclear. This may occur when there is early (subclinical) hypothyroidism, secondary hypothyroidism (sick euthyroid), anti-T4 antibodies or other causes of thyroid hormone suppression. In these situations a fT4 is a secondary test to help indicate the animal’s thyroid status. In some instances early hypothyroidism (subclinical) or unclear results may occur, a rational approach would be to retest the animal in 4 weeks time.

Other Factors Altering Thyroid Function Test Results

Besides sick euthyroid syndrome there are additional factors, which alter the results of thyroid function tests, potentially resulting in a misdiagnosis. The majority of factors reported cause an artificial decrease in thyroid hormone levels. Many drugs affect thyroid hormone levels and may result in the animal developing clinical signs of hypothyroidism. The exact mechanisms for each factor are not completely and individually understood. However, decreased binding of thyroid hormone to proteins and the ability of certain drugs to bind iodine, making it less available for thyroid hormone synthesis, are two mechanisms explaining how certain drugs cause a decrease in thyroid hormone levels. Sulfonamides, glucocorticoids, phenobarbital, clomipramine and NSAIDs have all been reported to decrease circulating thyroid hormone levels in animals. Sulfonamides inhibit thyroid peroxidase and decrease iodine organification and thus production of T3 and T4. This effect is noted to occur within weeks of therapy and its effect disappears 2 weeks after therapy has been discontinued.59 Glucocorticoids inhibit the entire...
hypothalamic-pituitary-thyroid axis and have a direct effect against thyroid hormone. The effects of phenobarbital are noted only in animals receiving long-term treatment. In order to produce reliable results, patients should not be receiving phenobarbital for 4 weeks prior to thyroid function testing. Various studies have found the influence of NSAIDs to be variable depending on the specific agent used. For animals receiving any of these medications, evaluation of thyroid function must be made with caution and preferably after having been taken off of the medications well in advance of testing.

Another factor well documented to result in lower thyroid hormone levels is athletic conditioning and training. Several studies have demonstrated well conditioned sled dogs and Greyhounds will reliably have lower TT4 and fT4, which may lead to a misdiagnosis of hypothyroidism. Finally, recent vaccination has been demonstrated to cause a transient increase in circulating autoantibody levels. This situation may cause a truly hypothyroid animal to appear euthyroid and may result in a delay or discontinuation of appropriate therapy. Thyroid function testing should not be completed when there is a history of vaccination within the previous 2 weeks.

**Treatment and Therapeutic Monitoring**

Supplementing synthetic thyroid hormone easily treats hypothyroidism. Levothyroxine sodium is available both as a human and veterinary product. It is recommended to avoid generic forms of the drug as studies in people have demonstrated wide variability in the bioavailability of the generic forms. If a generic form is used it is important to always prescribe the same formulation for an individual patient. Hormone supplementation is usually started at 0.02 mg/kg given orally twice daily. Rechecking thyroid function tests is recommended 6 weeks after therapy has begun. TT4 should be monitored and timed so that blood is taken six hours after pill administration. In stable well controlled animals, the total treatment may be given once daily with excellent clinical results, as long as adequate peak hormone concentrations are achieved. In animals receiving supplementation once daily, blood should be taken immediately before the medication is given and then again 6 hours later. When therapy is appropriate, TT4 levels should be high normal to high. If the TT4 level is significantly increased above normal, the medication dose should be decreased or the frequency changed. If the TT4 is low, then an increase in the dosage may be necessary. Prior to increasing the dose the clinician must assess client compliance, assure there are no GI issues that may impact absorption and confirm there has been no switch in levothyroxine formulation. Supplementation levels can be increased to a maximum of 0.8 mg per dog per treatment. It should be noted that levothyroxine doses given to dogs are in excess of those given to people and may cause confusion with pharmacists or even with human endocrinologists. Thyroid function should be monitored every 6 to 8 weeks for the first 6-8 months of treatment and then once to twice yearly.

Evaluation of TSH is a controversial tool to help assess response to therapy. In a well controlled animal, the TSH level would be expected to be in the normal range. However, there is a report indicating that TSH may be normal in as many as 75% of dogs requiring an increase in their supplementation levels. An increased TSH level is a predictable indicator of the need to increase supplementation levels in order to achieve adequate hormone
control. However a normal TSH level alone can not be interpreted, in all dogs, to indicate that hormone supplementation is adequate.\textsuperscript{72}

An important aspect to help assess the response to therapy is the degree to which clinical signs of hypothyroidism resolve. Marked improvement should be seen in attitude, activity level and alertness within one week of starting therapy. Polyneuropathy will usually start to improve quickly but complete resolution may take several months.\textsuperscript{29} The hematocrit and serum cholesterol level should gradually resolve in the first weeks of therapy.\textsuperscript{72} Dermatologic abnormalities will slowly improve with complete resolution usually taking up to 3 months.\textsuperscript{1,72} Response to treatment is a valuable tool to help determine the success of therapy, but should not replace appropriate blood tests. Hypothyroidism can be easily and successfully controlled and the prognosis for affected animals, when appropriately treated, is excellent.

**Myxedema Coma**

Myxedema coma is a very rare, life threatening, extreme manifestation of severe hypothyroidism and is considered an endocrine emergency. Mortality in people ranges from 15 to 60\%.\textsuperscript{32,73} Myxedema coma is rare in animals and much of what is known in veterinary medicine is based on a few case reports\textsuperscript{23,74} or is taken from human medicine. Myxedema coma must have a precipitating event, overwhelming normal homeostatic mechanisms. In people this is often an infection\textsuperscript{32} while in animals no single event has been repeatedly identified.

The common findings in myxedema coma are changes in mental status, altered thermoregulation and non-pitting skin edema.\textsuperscript{8,23,73,74} Mentation changes can range from altered alertness to coma. Coma does not always exist, and in people, mental depression is the most common assessment of mental status.\textsuperscript{32} Edema, localizing in the brain, is responsible for the development of altered mentation. Hyponatremia can cause a further decrease in neurological status.\textsuperscript{32} In myxedema coma, animals are often noted to be hypothermic but not shivering. Thyroid hormone has a permissive effect on calcium ATPase. In the hypothyroid state there is decreased activity of this enzyme which results in a decrease in ATP utilization.\textsuperscript{73} ATP is the powerhouse of the cell and with decreased activity there is decreased oxygen consumption and thus a decrease in heat generation. Additionally, hypothalamic dysfunction, secondary to edema formation in the brain, may lead to an alteration in the thermoregulatory set point.\textsuperscript{32,73} These changes may result in a lower body temperature and a reduced likelihood to shiver. Shivering can be stimulated from the hypothalamus or by the sympathetic nervous system. Thyroxine amplifies catecholamine function which helps to stimulate muscular activity associated with shivering,\textsuperscript{74} therefore a reduced T4 level will blunt the ability to shiver. Hypothermia reduces platelet function, which results in hepatic platelet sequestration and a decrease of enzymatic activity within the coagulation cascade.\textsuperscript{74} With a decreased body temperature there is peripheral vasoconstriction and central shunting of blood. Non-pitting edema of the skin is due to the deposition of glycosaminoglycans in the interstitial space.\textsuperscript{1,73}

Initial laboratory tests will reveal hypercholesterolemia, hypertriglyceridemia, hypoglycemia, anemia, hyponatremia, hypoxemia and hypercarbia.\textsuperscript{73,74} Thyroid function tests will be indicative of severe hypothyroidism with low TT4, low fT4 and elevated TSH.\textsuperscript{74} After a diagnosis of myxedema coma has been made, immediate treatment is necessary (Table Four). This usually means initiating treatment before thyroid function tests have returned to confirm the clinical suspicion of myxedema coma. Initial attention must be paid
to the provision of a patent airway and resuscitation of hypotension. Mechanical ventilation, described in people and dogs, may be necessary.\textsuperscript{33,73} The goals of fluid therapy are to support blood pressure and to address the decreased sodium levels. Clinicians must remember patients with myxedema coma have a decreased ability to clear free water. The hallmark of therapy is the provision of synthetic thyroid hormone intravenously. An IV levothyroxine dose of 5 $\mu$g/kg given twice daily is most commonly described.\textsuperscript{1,2,73} A more conservative replacement dose should be used when there is concern about cardiac function, especially the heart’s ability to deal with a sudden and rapid increase in metabolic rate.\textsuperscript{73,74} Rapid rewarming of the patient with myxedema coma must be avoided, as this may result in peripheral vasodilatation, hypotension and potential cardiovascular collapse. Correction of hypothermia should be passive and occur over a number of hours.

The greatest challenge with treating myxedema coma is recognizing the syndrome. Once recognized, immediate and intensive supportive care is necessary in order to treat the patient. Successful treatment has been reported in dogs and people,\textsuperscript{33,74} however mortality rates can be high.\textsuperscript{32}

\textbf{Conclusion}
Hypothyroidism is a common endocrine disease of dogs and is rare in cats. The most common forms of hypothyroidism are lymphocytic thyroiditis and idiopathic thyroid atrophy. The clinical signs of the disease are vague and can affect many body systems. Total T4 is considered an excellent screening test. Evaluation of cTSH is a good confirmatory test and when used in conjunction with TT4 or fT4 has a specificity of 98%. Several factors may alter the results of thyroid function testing. The presence of anti-T4 antibodies can falsely increase TT4 levels and mask true hypothyroidism. Alternatively many drugs and athletic conditioning, in some species, may decrease TT4 levels while not being associated with a true hypothyroid state. Treatment of hypothyroidism is easily achieved with levothyroxine supplementation. Success of therapy must be assessed with close monitoring of thyroid function tests. With appropriate treatment, hypothyroidism can be well managed with an excellent prognosis. A rare complication of severe hypothyroidism is myxedema coma. This condition is difficult to recognize but is associated with an altered mental state, hypothermia without shivering and non-pitting skin edema. With aggressive supportive therapy and IV thyroid hormone replacement, this condition may be successfully treated, though mortality remains high.
Table Three: Comparison of Canine Thyroid Diagnostic Tests (%)

<table>
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<tr>
<th></th>
<th>TT4 Sens</th>
<th>TT4 Spec</th>
<th>fT4(ED) Sens</th>
<th>fT4(ED) Spec</th>
<th>FT4 CLIA Sens</th>
<th>FT4 CLIA Spec</th>
<th>TSH Sens</th>
<th>TSH Spec</th>
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<td>81.8</td>
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</tbody>
</table>

TT4: Total thyroxine; fT4(ED): free T4 by equilibrium dialysis; TSH: thyroid stimulating hormone; Sens: Sensitivity; Spec: Specificity

a Peterson et al44
b Dixon et al45
c Ferguson et al75

Can we add a notation here that Peterson's study used the assay made by Nichols Institute which they no longer make


UNUSUAL THYROID DISORDERS
(FELINE AND CANINE HYPERTHYROIDISM)
Deborah S. Greco DVM, PhD

DEFINITION/OVERVIEW

• Feline hypothyroidism - Low to non-existent circulating levels of serum thyroxine caused by failure of the thyroid gland to secrete hormone or failure of the pituitary gland to secrete thyroid stimulating hormone.
• Canine hyperthyroidism - High circulating levels of serum thyroxine caused by a thyroid tumor (usually adenoma) or by feeding of exogenous thyroid tissue (treats, food)

ETIOLOGY/PATHOPHYSIOLOGY

Feline Hypothyroidism

• Acquired hypothyroidism is most commonly associated with radioactive iodine therapy, surgery or medical treatment for hyperthyroidism. Rarely, lymphocytic (autoimmune) thyroiditis similar to that seen in dogs with hypothyroidism is observed.
• Congenital hypothyroidism in cats is more common than acquired and may be caused by aplasia or hypoplasia of the thyroid gland, thyroid ectopia, dyshormonogenesis, maternal goitrogen ingestion, maternal radioactive iodine treatment, iodine deficiency (endemic goiter), hypopituitarism, isolated thyrotropin deficiency, hypothalamic disease, or isolated TRH deficiency

Canine Hyperthyroidism

• Thyroid tumor (rare, usually adenoma)
• Exogenous thyroid tissue in food or treats (usually raw)

SIGNALMENT/HISTORY

• Congenital feline hypothyroidism is seen in young animals usually less than 1 year of age.
• Acquired feline hypothyroidism is seen in older cats (more than 8 years of age) treated for hyperthyroidism
• Immune mediated hypothyroidism is seen in young to middle age cats.

Risk factors
• *Feline hypothyroidism* - Radioactive or surgical treatment for hyperthyroidism
• Canine hyperthyroidism - Feeding of treats or pet foods containing thyroid tissue

CLINICAL FEATURES

Feline
• Disproportionate dwarfism,
• Large birth weight
• Weakness
• Mental dullness
• Hypotonia
• Delayed dental eruption
• Lethargy
• Inappetence,
• Constipation
• Dermatopathy

Canine

• Polydipsia/polyuria
• Hyper excitability
• Polyphagia
• Behavior changes

Physical examination findings

Feline
Hypothermia
Abdominal distension
Macroglossia,
Midface hypoplasia, broad nose, and a large protruding tongue
Effusions of the body cavities (myxedematous fluid accumulation)
Retained puppy haircoat
Thinning of the haircoat
Ataxia

Canine
Hyperactivity
Tachycardia
Seizures
DIFFERENTIAL DIAGNOSIS

*Feline*
- Congenital hypothyroidism
- Pituitary dwarfism
- PSS
- Congenital renal disease
- FIP
- Acquired hypothyroidism

*Canine*
- Other causes of PU/PD (Cushings, DI, etc)
- Other causes of liver enzyme elevation (Hepatopathy, etc)
- Other causes of hyper excitability (Pheochromocytoma)

DIAGNOSTICS

**Minimum data base**

*Feline*
- Mild normocytic normochromic anemia
- Hypercholesterolemia, hypercalcemia

*Canine*
- Polycythemia (increased PCV)
- Increased liver enzymes (ALT, AST)

**Radiographs**

*Feline congenital hypothyroidism* - Epiphyseal dysgenesis

**Thyroid hormone measurement**

*Feline hypothyroidism*
- Low normal or low TT4 and or FT4 for the age of the kitten
  - Normal kittens aged 5-6 weeks, have serum total thyroxine (TT4) 2-3 times higher than normal adults.
- Low FT4 in a cat
- Endogenous cTSH - High

*Canine hyperthyroidism*
- High TT4 and FT4
- Low endogenous cTSH

**Pathological Findings**

*Feline*
• Goiter—enlarged thyroid gland filled with colloid
• Lymphocytic thyroiditis
• Congenital aplasia
  *Canine*
  • Thyroid adenoma

**THERAPEUTICS**

**Drug(s) of Choice**
Levothyroxine 0.1 mg per cat once or twice (kittens) daily

**Precautions / Interactions**
Avoid generic levothyroxine

**Alternative Drugs- NA**

**Diet**
*Canine* - discontinue diet or treats containing thyroid tissue

**Surgical Considerations**
Not applicable

**COMMENTS**

**Client Education**
*Feline*
  • Life long therapy will be required in congenital and autoimmune hypothyroidism
  • 50% of cats with acquired hypothyroidism will revert to normal within 6 mo to a year

*Canine*
  • Feed commercial pet food and treats from major manufacturers

**Patient Monitoring**
• Growth should normalize in congenital cases
• Every month initially and then every 6 months

**Prevention / Avoidance**

• *Feline*
  • Avoid goitrogens
  • Adjust radioactive iodine dosage and tailor to individual patient

• *Canine*
  • Avoid raw or homemade treats and pet food
AUTOIMMUNE POLYGLANDULAR SYNDROME
Deborah S. Greco

DEFINITION

- Autoimmune polyglandular syndromes (APS) include: APS Type 1 (diabetes, ectodermal mucositis, etc), APS Type 2 (hypoadrenocorticism, hypothyroidism, type 1 diabetes mellitus, premature ovarian failure), and APS Type 3 (liver cirrhosis plus endocrinopathies).

- Autoimmune polyglandular syndrome type II is defined as the occurrence of two or more of the following disorders in the same individual; adrenal insufficiency, primary hypothyroidism, insulin dependent diabetes mellitus (IDDM), primary hypogonadism (premature ovarian failure, immune mediated orchitis), myasthenia gravis, IMHA, ITP, hypoparathyroidism, hypopituitarism, and celiac disease.

ETIOLOGY/PATHOGENESIS

- Circulating organ specific autoantibodies are commonly present in APS type 2. Environmental factors combined with an HLA-associated genetic predisposition are thought to trigger the process. Cell-mediated immune abnormalities in the Type II syndrome include defects and alterations of cell surface markers, but the most consistent abnormality is a functional defect leading to a decrease in suppressor T cell activity.

- Approximately 45% of all patients with idiopathic (autoimmune) adrenal insufficiency will develop one or more additional endocrinopathies (usually hypothyroidism). APS II is inherited as an autosomal dominant trait in humans associated with the presence of human leukocyte antigens (HLA).

- Hypothyroidism is the most common initial endocrinopathy in the dog.

- Hypoadrenocorticism is usually followed by the development of hypothyroidism, but some dogs will develop hypoadrenocorticism instead. All three endocrinopathies in a single dog is rare.
• Type 1 diabetes combined with immune mediated thyroid disease (Hashimoto’s thyroiditis) is the most common initial endocrinopathy in humans and dogs.

• In a retrospective of 225 cases of canine hypoadrenocorticism, 4% of the dogs also suffered from hypothyroidism, 2 dogs had concurrent IDDM and hypoadrenocorticism, and one had concurrent hypoadrenocorticism, hypothyroidism, IDDM and hypoparathyroidism.

• Another retrospective of 45 dogs with adrenal insufficiency reported 4 dogs with concurrent hypothyroidism, one dog with concurrent IDDM and one dog with concurrent primary gonadal hypoplasia.

• A single case of Type II APS has been described in a middle-age female dog presenting in a hypothyroid crisis; treatment of the hypothyroid state resulted in precipitation of the hypoadrenocorticism. The presence of serum autoantibodies to thyroid and adrenal tissue was observed in this dog as evidence of autoimmune polyglandular syndrome Type II.

**SIGNALMENT/HISTORY**

- Hypoadrenocorticism and hypothyroidism—mean age of onset of the disease was in young adulthood (5.4 years).

- Second endocrinopathy less than 1 year (hypoadrenal and hypothyroidism) or 18 months (IDDM and hypothyroidism) after the first endocrinopathy.

- Slight female predilection

**CLINICAL FEATURES**

• Dogs diagnosed with hypoadrenocorticism, most common clinical signs include:

  • Lethargy
• Collapse
• Vomiting
• Weight loss
• Weakness
• Ataxia
• Anorexia
• Bradycardia
• Megaesophagus
• Diarrhea

• A decreasing insulin requirement is often the earliest sign of adrenal insufficiency

• Concurrent hypothyroidism and IDDM often have increasing insulin requirements as hypothyroidism may cause insulin resistance.

• In dogs diagnosed with hypopadrenocorticism as the initial endocrinopathy, thyroid evaluation was performed because of:
  • Continued lethargy despite adequate mineralocorticoid replacement therapy
  • Persistent hyponatremia and/or hypercholesterolemia
  • Dermatologic disease
  • Bradycardia
  • Obesity
  • Heat-seeking behavior.

**DIFFERENTIAL DIAGNOSIS**

• Inadequate glucocorticoid or mineralocorticoid supplementation in dogs with hypoadrenocorticism
• In dogs with diabetes mellitus, rule out other causes of insulin resistance

• In dogs with hypothyroidism, rule out other causes of weakness or electrolyte disturbances (e.g. hyperkalemia)

DIAGNOSTICS

• CBC/Chemistry profile/Urinalysis abnormalities
  
  • Hyponatremia
  • Hypercholesterolemia
  • Hyperkalemia
  • Hypochloremia
  • Azotemia
  • Hypocalcemia
  • Hypercalcemia

• ACTH response test

• Serum TT4 and endogenous canine TSH

• Acetycholine receptor antibody titer

THERAPEUTICS

Drug(s) of Choice
Levothyroxine 22-44 microgram/kg/day
Deoxycorticosterone pivilate 1 mg/kg IM q 25-30 days

COMMENTS

Client Education

• See hypoadrenocorticism client handout
Patient Monitoring

- Serum potassium and sodium
- Post pill TT4 or cTSH levels

SUGGESTED READING


