

Endocrinology

A COMPENDIUM OF LEADING ARTICLES IN THE FIELD OF VETERINARY ENDOCRINOLOGY SELECTED FOR THE VETERINARY PRACTITIONER

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Ultrasonography of the Thyroid

Bromel C, Pollard RE, Kass PH, et al. Ultrasonographic evaluation of the thyroid gland in healthy, hypothyroid, and euthyroid golden retrievers with nonthyroidal illness. J Vet Intern Med 2005;19:499-506.

► INTRODUCTION:

Background: Diagnosis of hypothyroidism is complicated by a variety of factors that affect thyroid function tests. These include unique breed characteristics, exercise, administration of certain drugs, and nonthyroidal illness.

In some circumstances, these factors could result in test results identical to those of a hypothyroid dog. In humans, thyroid gland ultrasound is frequently used to assess the gland in cases of suspected thyroiditis or gland enlargement. Ultrasonography is also used for guiding fine needle aspirates and biopsies of the gland. Ultrasound of the normal thyroid gland has been described in dogs, but not in those with hypothyroidism.

Objectives: The objective of this study was to compare the ultrasonographic appearance of the thyroid gland in dogs with primary hypothyroidism, healthy dogs, and dogs with nonthyroidal illness as an aid for differentiating hypothyroidism from nonthyroidal illness.

✦ SUMMARY:

Methods: Thirty-six healthy, 11 hypothyroid, and 35 euthyroid golden retrievers with clinical findings suggestive of hypothyroidism but with normal thyroid function tests underwent ultrasound examination of the thyroid glands. Diseases found in the 35 euthyroid dogs included obesity, allergic dermatitis, peripheral neuropathy, otitis externa, cricopharyngeal dysmotility, laryngeal paralysis, and Horner's syndrome. Ultrasound examination was performed using a 10-5 MHz multifrequency linear array transducer using the larynx, trachea,

and carotid artery as landmarks. Thyroid glands were assessed for size, shape, echogenicity, and homogeneity. Thyroid function was assessed by measurement of serum concentrations of T_4 , fT_4 by equilibrium dialysis, canine-thyroid stimulating hormone (c-TSH), and thyroglobulin autoantibodies in all dogs.

Results: All hypothyroid dogs had serum T_4 and fT_4 concentrations below the reference range, four of 11 had an elevated c-TSH concentrations, and positive thyroglobulin autoantibody tests were present in three of 11 dogs. Serum T_4 , fT_4 , and c-TSH concentrations were within reference ranges in 29, 28, and 35 euthyroid dogs with nonthyroidal illness, respectively. Thyroglobulin autoantibodies were identified in three dogs with nonthyroidal illness and in none of the normal dogs. On ultrasound examination, the common shape of the thyroid glands in the longitudinal axis was fusiform in all groups of dogs. Less frequently, the shape was elliptical. Hypothyroid dogs were more likely than euthyroid dogs to have a thyroid described as round or oval shape on transverse imaging. The mean length, height, width, and area of the thyroid gland were significantly less in hypothyroid dogs than both groups of euthyroid dogs, while no difference was noted between measurements in normal dogs and those with nonthyroidal illness. Despite the statistically significant reduction in thyroid gland volume between healthy and hypothyroid dogs, there was considerable overlap in measurements between these groups. When a reference range of mean ± 2 standard deviations of the thyroid gland volume in normal

Thyroid gland ultrasound can be useful in differentiating some dogs with hypothyroidism from those with nonthyroidal illness

- ▶ Ultrasonographic determination of thyroid size and volume can aid in differentiating between hypothyroidism and euthyroid sick syndrome. *J Vet Intern Med* 2005;19:499-506.
- ▶ Thyroid sonography can be useful in differentiating canine hypothyroidism from euthyroid sick syndrome. *J Vet Intern Med* 2005;19:491-498.
- ▶ Thyroid scintigraphy may change after methimazole treatment. *Vet Radiol & Ultrasound* 2005;46:267-272.
- ▶ Levothyroxine administration does not alter von Willebrand factor concentration or activity in Doberman pinschers with von Willebrand disease. *J Vet Intern Med* 2005;19:523-527.
- ▶ Cats with bilateral hyperthyroidism are at significantly higher risk for post-radioiodine treatment hypothyroidism than cats with unilateral hyperthyroidism. *J Am Vet Med Assoc* 2005;227:263-267.
- ▶ Radioiodine therapy is recommended as an adjunct to surgery in treating invasive thyroid carcinoma in dogs or as sole therapy when surgery is not advisable. *Aust Vet J* 2005;83:208-214.
- ▶ Protein-losing enteropathy in dogs can cause low ionized serum calcium, low serum 25 hydroxy-vitamin D, and high plasma parathyroid hormone concentrations. *J Sm Anim Pract* 2005;46:345-351.
- ▶ Total or adjusted total serum calcium concentration cannot be used to accurately predict ionized serum calcium concentration in dogs. *Am J Vet Res* 2005;66:1330-1336.
- ▶ Cats with an insulinoma, adrenocortical adenoma, or parathyroid gland adenoma may have multiple endocrine neoplasia type I. *J Am Vet Med Assoc* 2005;227:101-104.
- ▶ Basal plasma insulin concentration and the homeostasis model assessment (HOMA) are the best predictors of insulin sensitivity in cats. *J Fel Med Surg* 2005;7:183-193.
- ▶ Home monitoring of blood glucose using lancets results in the measurement of higher blood glucose concentrations than that measured in a clinical environment. *J Fel Med & Surg* 2005;7:163-171.
- ▶ Continuous glucose monitoring with a sensor in the subcutaneous interstitial fluid provides more accurate interstitial fluid glucose curve than the traditional blood glucose curve obtained by multiple venapunctures. *J Fel Med & Surg* 2005;7:153-162.
- ▶ Hypoglycemia caused by metastatic insulinoma in a dog was controlled with streptozotocin and corticosteroids. *J Sm Anim Pract* 2005;46:247-250.
- ▶ Cosyntropin at 5 µg/kg, intravenously stimulates maximum secretion of cortisol, adrenocortical sex hormones, and adrenocortical steroid intermediates one hour after administration. *Am J Vet Res* 2004;65:1631-1633.
- ▶ Primary hyperaldosteronism in cats should be among the differential diagnosis list in cases of hypokalemic polymyopathy or systemic hypertension, or both, in middle-aged to elder cats. *J Fel Med & Surg* 2005;7:173-182.
- ▶ Adrenocortical tumors in dogs can produce combinations of excess glucocorticoids and mineralocorticoids. *J Am Vet Med Assoc* 2005;226:1662-1666.
- ▶ Hyperaldosteronism and hyperprogesteronism caused by an adrenocortical carcinoma has been reported in a cat. *J Vet Intern Med* 2005;19:355-358.
- ▶ Mitotane administration has been associated with bone marrow necrosis in dogs. *J Am Vet Med Assoc* 2005;227:263-267.

- ▶ Long-term glucocorticoid treatment in dogs increases the risk of acquiring a urinary tract infection. *J Am Vet Med Assoc* 2005;227:239-243.
- ▶ Spaying cats prior to a year of age significantly decreases their risk of developing mammary carcinoma later in life. *J Vet Intern Med* 2005;19:560-563.

Ultrasonography of the Thyroid

Continued from page 1

dogs was used, only four of the 11 hypothyroid dogs had a thyroid volume below this range. Thyroid glands in most normal and nonthyroidal illness dogs were hyperechoic or isoechoic in comparison with surrounding musculature. Hypothyroid dogs were significantly more likely to have hypoechoic thyroid glands than euthyroid dogs of either group, but the glands were hyperechoic or isoechoic in over 50% of the hypothyroid dogs.

Conclusions: Ultrasonographic determination of thyroid size and volume can aid in differentiating between hypothyroidism and euthyroid sick syndrome.

CLINICAL IMPACT:

This study showed that thyroid gland ultrasound can be useful in differentiating some dogs with hypothyroidism from those with nonthyroidal illness. If the thyroid gland size is less than the reference range, hypothyroidism is highly likely, although a normal measurement provides little useful information. Because only a small proportion of the dogs with nonthyroidal illness studied actually had thyroid function tests that would have potentially led to a misdiagnosis of hypothyroidism, the most appropriate population was not tested. Another factor that might make thyroid ultrasound less accurate in the general population is that all dogs evaluated were golden retrievers, resulting in less variability in measurements of thyroid gland size.



Thyroid Sonography

Reese S, Breyer U, Deeg C, et al. Thyroid sonography as an effective tool to discriminate between euthyroid sick and hypothyroid dogs. *J Vet Intern Med* 2005;19:491-498.

► INTRODUCTION:

Background: Nonthyroidal illness can cause a reduction in serum T_4 and free T_4 concentrations, and less frequently an increase in serum thyroid stimulating hormone (TSH). These changes are more likely to be found in dogs with severe illness or those with specific diseases such as hyperadrenocorticism. Diagnostic alternatives for assessing thyroid function in a dog with abnormal thyroid function tests and nonthyroidal illness include a TSH response test or ultrasound examination of the thyroid glands.

Objectives: The purpose of this study was to evaluate the utility of thyroid gland ultrasound for differentiation of hypothyroidism from nonthyroidal illness in dogs with serum T_4 or fT_4 concentrations below the reference range.

✦ SUMMARY:

Methods: Thyroid gland ultrasound was performed in 30 thyroglobulin autoantibody (TgAA) positive dogs, 23 TgAA negative dogs, 26 dogs with euthyroid sick syndrome, and 87 healthy dogs. Dogs with euthyroid sick syndrome had a low serum T_4 concentration with (15 dogs) or without (9 dogs) a decrease in fT_4 , or an increase in serum canine-TSH (2 dogs). Ultrasound examination was performed using a 6–9 MHz linear transducer in dogs weighing more than 25 kg and a 7–13 MHz linear transducer in dogs weighing less than 25 kg. Thyroid gland size, shape, echogenicity, and homogeneity were evaluated in all dogs. Thyroid gland volume was calculated using measurements of the length, height, and width of the glands. The maximal cross sectional area and the thyroid gland volume were related to the estimated body surface area to compensate for differences in size of

dogs. The relative echogenicity of the thyroid glands was determined by comparing it to that of the sternothyroid muscle using image analysis software.

Results: The shape of the maximum cross sectional area was triangular or polygonal in the majority of the normal and euthyroid sick dogs while it was oval in most hypothyroid dogs. The thyroid gland volume and maximum cross sectional area were significantly less in hypothyroid dogs than either group of euthyroid dogs. The thyroid echogenicity was homogenous and hyperechoic compared with the sternothyroid muscle in normal and euthyroid sick dogs. The relative echogenicity was significantly lower in hypothyroid dogs compared with both groups of euthyroid dogs. Thyroid ultrasound in hypothyroid dogs with TgAA was most often homogeneously hypoechoic while that in 10 of the TgAA negative dogs showed a heterogenous echogenicity. No significant difference in any of the ultrasound measurements was found when normal control dogs and euthyroid sick dogs were compared.

When cutoff values were chosen to maximize sensitivity and specificity for hypothyroidism, the thyroid gland volume indicated hypothyroidism with a sensitivity of 81%, specificity of 96%, and accuracy of 91%. The maximum cross sectional area revealed a sensitivity of 77%, specificity of 96%, and accuracy of 90%. And, the relative echogenicity revealed sensitivity of 75%, specificity of 80%, and accuracy of 80%. The highest sensitivity (98%) was found when the thyroid gland volume and echogenicity were combined.

Conclusions: Thyroid gland ultrasound examination is an effective tool to differenti-

ate dogs with primary hypothyroidism from those with abnormal thyroid function tests due to nonthyroidal illness.

🌐 CLINICAL IMPACT:

This study was more effective in using thyroid gland ultrasound to differentiate hypothyroidism from euthyroid sick syndrome than similar studies. This may in part be because multiple breeds were studied and correction for metabolic body weight was made. It is possible that the golden retrievers used in a similar study with poorer results have a different pathogenesis of hypothyroidism than other breeds, although this seems unlikely.

When possible, testing thyroid function after resolution of the nonthyroidal illness provides the most accurate measure of thyroid function and would be preferred to thyroid ultrasound. Because the histologic appearance of thyroid glands from dogs with severe nonthyroidal illness has been shown not to differ from normal dogs, it is not surprising that abnormalities of the ultrasound appearance of the thyroids in dogs with euthyroid sick syndrome was not found in this study.

Thyroid gland ultrasound examination is an effective tool to differentiate primary hypothyroidism from abnormal thyroid function due to nonthyroidal illness



Effect of Methimazole on Thyroid Scans

Fischetti AJ, DiBartola SP, Chew DJ, et al. Effects of methimazole on thyroid gland uptake of ^{99m}Tc-pertechnetate in 19 hyperthyroid cats. *Vet Radiol Ultrasound* 2005;46:267-272.

► INTRODUCTION:

Background: Methimazole is often administered to hyperthyroid cats as a temporary means of control prior to scintigraphy, radioiodine treatment, or thyroidectomy. Methimazole blocks thyroid hormone synthesis, but does not affect iodide uptake. The administration of methimazole prior to thyroid scans or radioiodine treatment for hyperthyroidism is generally believed to have no effect on the scans or on response to radioiodine. However, the incidence of hypothyroidism after radioiodine therapy in cats is surprisingly high and may be related to recent methimazole treatment.

Objectives: The purposes of this study were to identify changes in thyroid-to-salivary ratios (T:S), percentage of thyroid uptake of technetium, and serum canine-thyroid stimulating hormone (c-TSH) concentration in hyperthyroid cats made euthyroid by a month of methimazole treatment and to correlate the changes in the scintigram with serum c-TSH concentration.

✕ SUMMARY:

Methods: Thyroid scintigraphy was performed on 19 hyperthyroid cats before and after about one month (36 ±6 days) of methimazole treatment (2.5 mg, per os, twice per day). The T:S ratio and the percentage thyroid uptake 20 and 60 minutes after the injection of technetium pertechnetate were compared before and after methimazole treatment. Serum c-TSH concentration was determined before and after methimazole administration.

Results: The thyroid uptake of technetium was positively correlated with serum T₄ before treatment with methimazole. Serum c-TSH concentration was suppressed, and this was not changed with methimazole treatment

in 17 cats. The two cats with an increase in c-TSH concentration also had unilateral thyroid uptake on initial evaluation but bilateral, asymmetrical technetium uptake after methimazole treatment. Thyroid scintigraphy did not significantly change after methimazole treatment.

A month of methimazole treatment can alter the scintigram

Conclusions: Determination of serum c-TSH concentration may be helpful in identifying methimazole-induced scintigraphic changes of the thyroid in mildly hyperthyroid cats.



CLINICAL IMPACT:

This study unequivocally demonstrates that some cats (2 among 19) have growth in normal follicular cells during a month of methimazole treatment which can alter the scintigram and should render normal thyroid cells undesirably susceptible to radioiodine treatment damage. The two cats previously mentioned had scintigrams consistent with unilateral hyperthyroidism which appeared after methimazole treatment to be bilateral hyperthyroidism.

Methimazole treatment is valuable in assessing the ability of hyperthyroid cats to tolerate euthyroidism without going into decompensated renal failure. However, a period of equilibration after methimazole trial should be provided prior to radioiodine treatment or prior to scintigraphy to decide whether a unilateral or bilateral thyroidectomy is indicated.

The authors' conclusion of this study was that c-TSH concentration should be determined in hyperthyroid cats because some methimazole treated cats that have serum c-TSH increases may have altered thyroid scintigraphy. Based on the c-TSH concentrations, only two cats among 19 in this study had an increase in c-TSH after suppressing serum T₄ with methimazole. However, all cats were considered to have normal c-TSH concentra-

tions (0-21 mU/l) prior to methimazole when the median serum T₄ concentration was 7.0 µg/dl (range 4.2-15 µg/dl). When serum T₄ is abnormally elevated (more than 4 µg/dl), serum feline-TSH should not be measurable. The TSH assay used in this study for cats was a commercial immunoradiometric assay for canine TSH. The value of measuring c-TSH in cats after methimazole treatment of hyperthyroidism is questionable.



Thyroid Hormone Effects on Hemostasis

Heseltine JC, Panciera DL, Troy GE, et al. Effect of levothyroxine administration on hemostatic analytes in Doberman pinschers with von Willebrand disease. *J Vet Intern Med* 2005;19:523-527.

► INTRODUCTION:

Background: Von Willebrand disease (vWd) is the most common congenital bleeding disorder in dogs. Type I is a quantitative decrease in vW factor (vWf) with a normal multimeric pattern. Many dog breeds are affected, including Doberman pinschers in which the incidence may be 70%. Manifestations may range from subclinical to severe bleeding tendency. Suggested treatment options are desmopressin, cryoprecipitate, or levothyroxine. However, the efficacy of levothyroxine in treating vWd is questionable.

Objectives: The purpose of this investigation was to determine if levothyroxine supplementation sufficient to induce mild hyperthyroidism in euthyroid Doberman pinschers with severe vWd would increase vWf:Ag or vWf function.

✕ SUMMARY:

Methods: Eight euthyroid Doberman pinschers with vWd (vWf of less than 15% of normal) were administered 0.04 mg/kg, per os, twice per day, or a placebo in a two period, two treatment, double-blinded crossover with 30 day washouts between treatments. Buccal mucosal bleeding time, plasma vWf concentration, vWf collagen binding activity, factor VIII coagulant activity, and serum total T₄, free T₄ (fT₄), T₃, and canine-thyroid stimulating hormone (c-TSH) concentrations were measured on days 0, 2, and 30 of each treatment cycle.

Results: The concentration of vWf and activity of vWf collagen binding were markedly low (mean of 8.9% and 11.1%, respectively). The responses to levothyroxine and placebo were not significantly different on any day or for any parameter other than serum thyroid

hormone concentrations. On days 2 and 30, dogs administered levothyroxine had significantly higher serum T₄, fT₄, and T₃ concentrations and significantly lower c-TSH concentration.

Despite marked increase in circulating levothyroxine, no change in bleeding time, vWf concentration, or vWf function occurred

Conclusions: Levothyroxine supplementation to euthyroid Doberman pinschers with vWd had no direct effect on plasma vWf concentration or activity.



CLINICAL IMPACT:

The dosage of levothyroxine in this study was higher than a replacement dose for a total deficiency of thyroid hormone production. As expected, mild hyperthyroidism resulted with serum T₄ levels approximately twice the upper limit of normal concentration. Despite marked increase in circulating levothyroxine, no change in bleeding time, vWf concentration, or vWf function occurred.

No adverse effect of administered levothyroxine was noted in a month of treatment. However, if one assumed that levothyroxine could be beneficial in vWd, life-long treatment would be appropriate. Long-term (more than a month) administration of slightly excessive levothyroxine in humans can cause depletion of hepatic and skeletal muscle glycogen and calcium depletion.

Evidence for a benefit in treating vWd with levothyroxine is lacking. Adverse effects of long-term treatment, in addition to the unnecessary expense, are possible.



Post-Radioiodine Treatment Hypothyroidism in Cats

Nykamp SG, Dykes NL, Zarfoss MK, et al. Association of the risk of development of hypothyroidism after iodine 131 treatment with the pretreatment pattern of sodium pertechnetate Tc 99m uptake in the thyroid gland in cats with hyperthyroidism: 165 cases (1990-2002). J Am Vet Med Assoc 2005;226:1671-1675.

► INTRODUCTION:

Background: Radioiodine is often considered the best treatment for hyperthyroidism in cats. Between 5 to 18% of hyperthyroid cats treated with radioiodine develop hypothyroidism based on serum T₄ concentrations after treatment. Normal thyroid tissue should be metabolically quiet during hyperthyroidism due to the subsequent negative feedback on thyroid stimulating hormone production. As such, normal thyroid tissue should be relatively refractory to the tissue destruction of radioiodine. Approximately 30% of hyperfunctioning thyroid tumors are unilateral. Scintigraphy results prior to treatment with radioiodine might provide an indication of the risk of post-treatment hypothyroidism.

Objectives: The objective of this study was to determine if the risk of developing hypothyroidism after treatment of hyperthyroidism in cats with radioiodine is associated with the pretreatment scintigraphy results.

✕ SUMMARY:

Methods: The medical records of 165 hyperthyroid cats that undergone scintigraphy prior to radioiodine therapy were reviewed along with a referring veterinarian questionnaire for post-treatment results. Parameters assessed were scintigraphy findings, serum T₄ concentration before and after treatment prior to discharge from the hospital, and serum T₄ concentration at least three months after discharge.

Results: Thirty percent of radioiodine treated cats (50 of 165) developed laboratory (subnormal serum T₄ concentration) hypothyroidism. Among 109 with bilateral hyperthyroidism, 39 became hypothyroid. Ten of 50 cats with unilateral hyperthyroidism became hypothy-

roid post-treatment. Of six cats with multifocal involvement, one cat developed hypothyroidism. Cats with bilateral involvement had twice the risk of post-treatment hypothyroidism, compared to cats with unilateral hyperthyroidism based on scintigraphy.

Cats with bilateral hyperthyroidism have significantly higher risk of radioiodine induced hypothyroidism

Conclusions: Cats with bilateral hyperthyroidism based on scintigraphy have significantly higher risk of radioiodine induced hypothyroidism.



CLINICAL IMPACT:

Although 30% of radioiodine treated hyperthyroid cats developed subnormal serum T₄ concentrations after treatment, no adverse clinical signs consistent with hypothyroidism were described. Low serum T₄ concentrations immediately after destruction of hyperthyroid nodules are essential for a cat to become euthyroid later. Low serum T₄ promotes thyroid stimulating hormone secretion that induces the normal remaining thyroid tissue to become sufficiently functional for euthyroidism.

However, renal failure in a hyperthyroid cat can be compensated by the high glomerular filtration rate (GFR) promoted by hyperthyroidism. Treating hyperthyroidism can precipitate a crisis in renal function by a drop in GFR. It is reasonable to expect that cats at risk for post-radioiodine treatment hypothyroidism could be at greater risk for lower GFR and associated renal failure than those cats that become euthyroid with or without thyroid supplementation. The incidence of renal failure in post-treatment euthyroid and hypothyroid cats was not reported in this study. If the risk of renal failure is greater in hypothyroid cats, those at risk should be monitored and treated with replacement thyroxine as soon as serum T₄ concentrations become subnormal.



Radioiodine Treatment of Canine Thyroid Carcinoma

Worth AJ, Zuber RM, Hocking M. Radioiodine (^{131}I) therapy for the treatment of canine thyroid carcinoma. *Aust Vet J* 2005;83:208-214.

► INTRODUCTION:

Background: Thyroid carcinoma is a malignancy that is often invasive and frequently metastasizes to regional lymph nodes and lungs. Prognostic indicators for survival after surgery include tumor size, histologic type, mobility of the tumor in the surrounding tissue, and the presence or absence of metastasis. Invasive carcinomas that are adherent to adjacent tissues carry a poor prognosis as surgery generally does not result in complete resection. External beam radiation has recently been shown to result in long-term survival of most cases regardless of the invasiveness of the tumor. Because most dogs with thyroid carcinoma do not secrete excessive amounts of thyroid hormone and thus do not develop hyperthyroidism, radioiodine treatment has been reported infrequently.

Objectives: The objective of this study was to evaluate the efficacy of radioiodine administration for treatment of thyroid carcinomas in dogs.

✕ SUMMARY:

Methods: Medical records of 65 dogs with a histological or cytological diagnosis of thyroid carcinoma were reviewed. Scintigraphy with technetium was performed in all dogs. Dogs with mobile tumors and without evidence of metastasis underwent surgical resection alone. Most dogs with mobile tumors and metastasis underwent surgical excision followed by radioiodine if technetium uptake was noted on scintigraphy. However, some were treated with radioiodine alone. In dogs with invasive tumors with or without metastasis, surgical debulking was performed in most followed by radioiodine treatment. Some dogs received

radioiodine treatment alone. Radioiodine was administered to 43 dogs, with the dosage ranging from 555 to 1850 MBq (15 to 50 mCi) ^{131}I . Levothyroxine supplementation was administered to 34 of the dogs after radioiodine treatment.

Results: Beagles and boxer dogs were the most common breeds affected, accounting for 12% and 11%, respectively. Of the 47 dogs with a histologic diagnosis, 38 were classified as follicular carcinomas or simply thyroid carcinoma.

Prior to treatment, serum T_4 was below the reference range in 14 and above the reference range in 11 of the 36 dogs tested. Clinical signs of hyperthyroidism were present in only two dogs. Seven dogs received no treatment, 15 underwent surgical excision only, 32 had radioiodine treatment alone, and 11 had a combination of surgery and radioiodine treatment.

The median survival time in the untreated group was three months, the radioiodine treatment group was 30 months, and the combined treatment group was 34 months. The median survival time of surgery alone was not determined because eight of the dogs died of causes unrelated to the thyroid carcinoma. Dogs that received no treatment had significantly shorter survival. Those dogs receiving only surgery had significantly longer survival than the median survival of all dogs, although no difference in survival was noted between any of the treatment groups. Stage of disease had no significant effect on survival, including dogs with distant metastasis.

Conclusions: Radioiodine administration is an effective treatment for thyroid carcinoma.

🌀 CLINICAL IMPACT:

The duration of survival after administration of radioiodine was somewhat shorter than that obtained using external beam irradiation. However, the cost and potential adverse

effects of radioiodine treatment are considerably less than those of external beam irradiation. Surgery remains the treatment of choice for freely mobile tumors. The prolonged survival times noted in this study in dogs with and without hyperthyroidism should prompt clinicians to consider radioiodine as a useful treatment modality whenever it is available.

Radioiodine is an effective treatment for thyroid carcinoma



Hypovitaminosis D and Protein-Losing Enteropathy

Mellanby RJ, Mellor PJ, Roulois A, et al. Hypocalcaemia associated with low serum vitamin D metabolite concentrations in two dogs with protein-losing enteropathies. J Sm Anim Pract 2005;46:345-351.

► INTRODUCTION:

Background: Serum calcium exists in three forms: ionized, protein-bound, and complexed. Approximate percentages of total serum calcium are 50% ionized, 40% protein-bound, and 10% complexed. The most common causes for hypocalcemia in dogs are renal failure, hypoalbuminemia, primary hypoparathyroidism, eclampsia, and pancreatitis. The cause of vitamin D deficiency can be dietary, intestinal malabsorption of fat, or impaired hydroxylation to active forms such as occurs with kidney failure.

Objectives: The purpose of this report was to describe the clinical, serum biochemical, endocrine, and necropsy findings of two dogs with protein-losing enteropathies and low plasma ionized calcium and vitamin D concentrations.

✕ SUMMARY:

Case Reports: Two dogs were presented with diarrhea and weight loss and diagnosed with protein-losing enteropathies. Both dogs had total and ionized hypocalcemia plus hypoalbuminemia. They also had increased plasma parathyroid hormone concentration and low serum 25-hydroxyvitamin D concentrations.

One dog was diagnosed with lymphangiectasia at necropsy. The other dog was diagnosed with chronic lymphocytic/plasmacytic enteritis and cystic mucoid changes using endoscopic biopsies of the duodenum.

Conclusions: These are believed to be the first reported cases of dogs having protein-losing enteropathies with ionized hypocalcemia, low plasma 25-hydroxyvitamin D and 1,25-dihydroxyvitamin D concentrations, and high parathyroid hormone concentrations.



CLINICAL IMPACT:

Intestinal absorption of dietary calcium is controlled to a major extent by vitamin D.

Dogs rely primarily on dietary sources of vitamin D since they are less

efficient in cutaneous production than are primates. Vitamin D is a fat-soluble vitamin. Fat must be absorbed from the intestine for dietary vitamin D to be absorbed.

Fat absorption tests were not reported in either of the cases of this report. Serum cholesterol was measured in one of the dogs and found to be abnormally low, nearly one-half the lower limit of normal on two occasions. Fat malabsorption and fat-related malabsorption of dietary vitamin D is very likely the cause for hypovitaminosis and a contributing cause, with hypoalbuminemia, to hypocalcemia in both reported dogs.

Fat malabsorption and fat-related malabsorption of dietary vitamin D is very likely the cause for hypovitaminosis



Prediction of Serum Ionized Calcium Concentration

Schenck PA, Chew DJ. Prediction of serum ionized calcium concentration by use of serum total calcium concentration in dogs. *Am J Vet Res* 2005;66:1330-1336.

► INTRODUCTION:

Background: The total calcium measured on standard serum biochemistry profiles is made up of ionized, protein bound, and complexed calcium. Ionized calcium is the biologically active form of calcium, and its relationship with total calcium can be altered by changes in concentrations of binding proteins, substances such as citrate and phosphates that form complexes with calcium, and blood pH. Adjustments of total calcium concentration for changes in total protein or albumin are commonly used to predict changes in ionized calcium. Unfortunately, they may be prone to error.

Objectives: The objective of this study was to determine accuracy of adjustments to total calcium concentration for changes in albumin and total protein with measurements of ionized calcium.

✕ SUMMARY:

Methods: Serum total calcium, ionized calcium, total protein, and albumin concentrations were measured in 1141 dogs without renal failure and in 490 dogs with renal failure. The serum total calcium concentration was adjusted for total protein and albumin concentrations using standard equations. Dogs were classified as normocalcemic, hypercalcemic, or hypocalcemic for each of the calcium variables based on laboratory reference ranges for ionized and total calcium. The adjusted calcium concentrations were classified using reference ranges for total calcium. The sensitivity, specificity, positive predictive value, negative predictive value, likelihood ratios, and diagnostic discordance were calculated using ionized calcium concentration as the correct measure of normo-

calcemia, hypercalcemia, or hypocalcemia. Comparisons were made with total and corrected serum calcium concentrations.

Results: Correlation between ionized calcium and all other measurements in all dogs was fair, with correlation coefficients ranging from 0.57 for total calcium to 0.73 for both adjusted calcium measurements. The correlation was slightly worse for dogs with chronic renal failure and slightly better for those without renal failure. Based on ionized calcium, 822 dogs were normocalcemic, 304 were hypercalcemic, and 507 were hypocalcemic. With regard to classification of normocalcemia, hypercalcemia, or hypocalcemia, overall agreement of total calcium with ionized calcium occurred in 73% of cases, calcium corrected for total protein in 63% of cases, and calcium corrected for albumin in 62% of cases.

Agreement was less for the subgroup of dogs with renal failure. The agreement between ionized calcium and total calcium was 74%, calcium adjusted for total protein was 47%, and 46% for calcium adjusted for albumin.

The sensitivity of total calcium in all dogs with hypercalcemia based on ionized calcium was 67%, with adjustments for both albumin and total protein increasing the sensitivity. The specificity of total calcium for hypercalcemia based on ionized calcium concentration was 98% in dogs without renal failure, but only 83% in those with renal failure. The adjusted calcium values were less specific, especially in dogs with renal failure. In dogs with hypocalcemia, total calcium had a sensitivity of 67%, while the total calcium in the subgroup of dogs with renal failure had a sensitivity of only 45%. Both adjustments for total calcium resulted in a marked reduction

in sensitivity of the test in hypocalcemic dogs. The sensitivity of total calcium for hypocalcemia as determined by ionized calcium was 91% in all dogs and was slightly higher (96%) in dogs with chronic renal failure.

Conclusions: Adjustment equations for total protein and albumin are of little use in improving the accuracy of predicting ionized calcium concentration.



CLINICAL IMPACT:

Correction of total calcium for total protein and albumin concentrations may result in misleading interpretations of results. With regard to hypercalcemia, results of this study suggest that if the total calcium is elevated the ionized calcium is very likely elevated as well. However, the strength of the association between total and ionized calcium is poor for dogs with chronic renal failure as might be expected due to the increase in the fraction of complexed calcium and alterations in serum protein concentrations in dogs with chronic renal failure. Measurement of ionized calcium can be readily accomplished with a number of point-of-care chemistry instruments that are practical for many veterinary hospitals.

Correction of total calcium for total protein and albumin concentrations may result in misleading interpretations



Multiple Endocrine Neoplasia Type I

Reimer SB, Pelosi A, Frank JD, et al. Multiple endocrine neoplasia type I in a cat. *J Am Vet Med Assoc* 2005;227:101-104.

► INTRODUCTION:

Background: Multiple Endocrine Neoplasia (MEN) is a group of multiglandular syndromes believed to be caused by an inherited loss of function of a tumor suppressor gene. Tumors begin to develop at the same time in endocrine organs with the same embryologic precursor in the neuroectoderm. The three most well defined types in humans are MEN types I, IIa, and IIb. Major components of MEN, type I tumors of the parathyroids, pituitary, and pancreatic islets. The most common tumors involved are chromophobe adenoma, gastrinoma, and multiglandular adenomas or hyperplasia.

Objectives: The reason for this report was to describe a cat with MEN, Type I.

✦ SUMMARY:

Case Report: A 13-year-old, castrated male, domestic long-hair cat was presented with a history of lethargy, exercise intolerance, and ventroflexion of the neck. Two years earlier, the cat had hyperthyroidism and underwent a unilateral (right) thyroidectomy/parathyroidectomy. Histologic examination of a removed parathyroid revealed an adenoma although serum calcium concentration was normal. Hypokalemia was found on recent serum biochemical evaluation of the cat. Potassium supplements were administered and signs of lethargy, exercise intolerance, and ventroflexion of the neck were initially controlled but returned within a few months.

Five months after the recent clinical signs were observed, a mass was palpated on the ventral aspect of the neck on the left side. Serum thyroid hormone concentrations were normal. Abnormal serum chemistry results included high calcium (11.3 mg/dl), hypoglycemia (38 mg/dl), and high sodium (163 mEq/L), and markedly high aldosterone

(1,741 pmol/L, reference range, 194-388 pmol/L). An assay for parathyroid hormone revealed elevated concentration (8.5 pmol/L, reference range, 0-4 pmol/L) concurrent with high serum ionized calcium (1.66 mmol/L, reference range, 1.0-1.4 pmol/L). Parathyroid hormone-related protein was unmeasurably low. Primary hyperparathyroidism was diagnosed based on inappropriately elevated parathyroid hormone concentration concurrent with hypercalcemia. In addition, primary hyperaldosteronism was diagnosed on the basis of markedly elevated and inappropriately high serum aldosterone concentration concurrent with hypokalemia.

Ultrasonography of the abdomen revealed that the left adrenal gland was enlarged. An exploratory laparotomy was performed. The liver appeared grossly normal but was biopsied. A 2 X 3 cm mass was seen in the right lobe of the pancreas, and a 2.5 X 3.0 cm mass was associated with the left adrenal gland. The pancreatic tumor was removed by a partial pancreatectomy, and a left adrenalectomy was performed. The pancreatic tumor was diagnosed histologically as an undifferentiated neuroendocrine islet cell tumor. The adrenal tumor was a cortical adenoma. Immunohistologic examination results were consistent with an aldosteronoma and an insulinoma.

Six days after discharge from the hospital, the cat was clinically improved and was returned for parathyroidectomy. A 1.2 X 0.8 cm mass was found on the caudal pole of the thyroid gland. A left thyroid/parathyroidectomy was performed. The tumor was histologically and immunohistologically diagnosed as a parathyroid adenoma. The cat was stabilized on declining calcitriol administration and thyroxine supplementation for at least six months postoperatively.

Conclusions: This was the first reported case of MEN, type I in a cat and was satisfactorily managed by the surgical excision of an aldosteronoma, insulinoma, and parathyroid adenoma.

🌀 CLINICAL IMPACT:

Without a familial history or demonstration of a chromosome mutation analogous to the defect in humans with MEN, type I, on the long arm of chromosome 11, the case of this report could have been an unrelated coincidence of tumors in an old cat. However with the paucity of reports of aldosteronomas, insulinomas, and parathyroid adenomas in cats, the chance of coincidental occurrence of all three in one cat would be extremely remote. Whenever MEN is diagnosed, family members should be screened by periodic monitoring serum calcium, blood glucose, and serum electrolytes, among other parameters related to endocrinopathies associated with MEN.

Whenever MEN is diagnosed, family members should be screened



Insulin Sensitivity in Cats

Appleton DJ, Rand JS, Sunvold GD. Basal plasma insulin and homeostasis model assessment (HOMA) are indicators of insulin sensitivity in cats. *J Fel Med Surg* 2005;7:183-193.

► INTRODUCTION:

Background: Cats with mild insulin resistance are at risk for developing impaired glucose tolerance as they gain weight. Increased insulin secretion is necessary in animals with glucose intolerance in order to maintain euglycemia. Theoretically, increased demand on beta-islet cells over a long period of time may lead to islet cell exhaustion, decreased insulin secretion, and ultimately, diabetes mellitus. It would be useful to have a method of determining insulin sensitivity that was practical for use in a clinical setting.

Objectives: The objective of this study was to determine a simple, practical method of assessing insulin sensitivity that could be used in veterinary clinics.

✕ SUMMARY:

Methods: Indices of insulin sensitivity were derived from computerized mathematical modeling of blood glucose and insulin concentrations. Indices obtained during an insulin-modified frequently sampled intravenous glucose tolerance test (FSIGTT) in 25 cats of ideal body weight were used to compare with insulin sensitivity derived from insulin and glucose concentrations. Reference ranges were derived from these cats.

The simple measures of insulin sensitivity were then calculated in cats that had been evaluated by the minimal model analysis in previous studies, including 32 cats that were underweight, normal weight, and overweight. These measures were also assessed in 16 obese cats, including seven with glucose intolerance. Standard intravenous glucose tolerance tests (0.5 g/kg) were also performed in all cats. Simple measures of insulin sensitivity

included basal insulin, basal glucose, insulin to glucose ratios, the mean of two basal samples obtained on different days. In addition, insulin sensitivity estimates were derived from glucose, insulin, or insulin-to-glucose ratios 60 and 120 minutes after glucose injection, area under the insulin curve, and ratio of area under the insulin-to-glucose curve during the standard glucose tolerance test. Other estimates of sensitivity derived by transformation of basal insulin and glucose concentrations were evaluated.

Results: The measure that correlated most closely with the FSIGTT-derived value for insulin sensitivity was the basal insulin concentration for both the 32 cats with variable body conditions and the obese cats with glucose intolerance. Other parameters that were nearly as well correlated were the basal insulin-to-glucose ratio, the insulin 60 minutes after glucose, and the homeostasis model assessment (HOMA) that uses the product of insulin and glucose concentrations divided by a constant. In the 32 cats with normal insulin sensitivity, correlation between FSIGTT-derived measures and the simpler estimates was moderate. In the seven obese cats with glucose intolerance, basal insulin, mean of two insulin samples, insulin-to-glucose ratio, and HOMA were correlated to a much greater degree than in the 32 cats with various body conditions. None of the simple estimates of insulin sensitivity were correlated with that obtained by minimal model analysis in the 25 ideal body weight cats.

Conclusions: The best simple measurement of insulin sensitivity in cats is basal plasma insulin concentration after a 12 hour fast.



CLINICAL IMPACT:

Simple estimates of insulin sensitivity and

glucose intolerance have been used successfully for evaluation of populations of humans. Their use in individuals is limited and generally much less accurate than more sophisticated measures of insulin sensitivity. The lack of correlation between any of the simple estimates and minimal model analysis in ideal body weight cats demonstrates a substantial limitation of the clinical utility of these estimates. Although basal insulin concentrations have been shown to predict the development of glucose intolerance during weight gain, basal insulin concentrations are highly variable in diabetic cats and do not predict response to oral hypoglycemic agents or recovery from diabetes mellitus.

While there appeared to be greater correlation in cats with glucose intolerance, there were only seven cats studied. Because correlation between the measurements was widely variable in different populations, use of estimates of insulin sensitivity such as basal fasting glucose for identifying cats at risk for developing glucose intolerance requires further study prior to their use in clinical cases. In addition, a link between glucose intolerance and development of diabetes mellitus remains to be shown in the feline population.

Use of estimates for identifying cats at risk for developing glucose intolerance requires further study



Home Monitoring of Diabetes Mellitus

Casella M, Hassig M, Reusch CE. Home-monitoring of blood glucose in cats with diabetes mellitus: evaluation over a 4-month period. *J Fel Med Surg* 2005;7:163-171.

► INTRODUCTION:

Background: New blood glucose monitors and lancet blood collection techniques have made home blood glucose monitoring more feasible for owners of diabetic cats. Assessment of glycemic control by detecting glucosuria is an insensitive and inaccurate means. Repeated venapunctures in a hospital causes stress which adversely affects the blood glucose concentration results and usefulness of the blood glucose curves. Veins crucial to management of ketoacidosis can be scarred and thrombosed, compromising quality of care in later stages of diabetes.

Although lancet collection of blood and home monitoring of blood glucose is preferable to in hospital monitoring, owner compliance can be a problem. Owners may be unwilling to perform the blood collection and testing, or they may be incompetent.

Objectives: The objectives of this study were to determine if owners of diabetic cats are willing and capable of performing long-term home monitoring, what problems are encountered, and the correlation between blood glucose curves determined at home and those determined in the hospital using the same assay technique.

✕ SUMMARY:

Methods: Fifteen diabetic cats were evaluated in the study. Re-evaluations were done at 1, 3, 6, 9, 12, and 16 weeks. Evaluations included updates of patient history, physical examination, hematocrit, serum fructosamine, albumin, and total protein. A blood glucose curve was determined on seven blood samples collected every two hours for 12 hours.

During the second evaluation, owners

were taught to do blood glucose determinations at home by lancing the inner side of the pinna using a vacuum lancet and measuring glucose using a reflectance colorimeter. One week prior to each re-evaluation in the hospital, owners were instructed to determine a blood glucose curve at home. Blood glucose curves determined at home and in the hospital at the 5th and 6th, 8th and 9th, 11th and 12th, and 15th and 16th weeks.

Results: Twelve of the 15 owners of the cats were able to collect and monitor blood glucose concentrations over four months. The most common problems were restraint of the cat and creating negative pressure needed to get a drop of blood. Problems were usually resolved with additional owner training. Blood glucose curves tended to be lower when determined in the hospital. Some differences were significant. If hospital blood glucose curves had been used exclusively, treatment decisions would have been different in 38% of cases.

Conclusions: Measurement of blood glucose in cats is feasible at home and enables frequent determinations of blood glucose curves.

CLINICAL IMPACT:

Blood glucose curves are not necessary to stabilize and manage every diabetic cat. Blood glucose curves can be helpful and should be performed in poorly regulated cases. Many of these cases will have sufficient complications or concurrent problems to require hospitalization.

Diabetic cats that were included in this study were owned by people who were willing to learn how to collect their cat's blood at home. Twelve owners were capable. Three were successful in their first attempt. It is undetermined how often owners of diabetic cats approached at random will be willing and capable of performing blood glucose

curves on their cat.

Having a willing and capable owner with a poorly regulated diabetic cat that does not require hospitalization perform blood glucose curves at home could be advantageous. However, the situation will not be frequent, and not all owners will be willing and capable.

The most common problems were restraint of the cat and creating negative pressure needed to get a drop of blood



Continuous Blood Glucose Monitoring in Diabetic Cats

Ristic JME, Herrtage ME, Walti-Lauger SMM, et al. Evaluation of a continuous glucose monitoring system in cats with diabetes mellitus. *J Fel Med Surg* 2005;7:153-162.

► INTRODUCTION:

Background: Measurement of serial blood glucose concentrations following insulin administration is a standard technique for assessing adequacy of treatment of diabetic patients. Shortcomings of this monitoring tool include the necessity of repeated venapunctures, stress associated with hospitalization, the potential for misleading information if samples are not obtained frequently enough, and the variability of results despite using a consistent insulin dose.

Technology for sampling the interstitial fluid glucose concentration using a disposable sensor implanted percutaneously is now available and has been documented to be accurate in canine and feline diabetics. The continuous glucose monitoring system consists of a sensor that is inserted subcutaneously using a percutaneous introducer, a monitor that records the interstitial glucose concentration every five minutes, and a docking station that allows the recorded information to be downloaded to a computer.

Objectives: The purpose of this study was to evaluate the utility of the Medtronic MiniMed Continuous Glucose Monitoring System (CGMS) in cats with diabetes mellitus.

✕ SUMMARY:

Methods: Fourteen cats with diabetes mellitus had interstitial glucose concentrations measured for 11.5 to 70 hours using the CGMS while hospitalized. All cats were considered sufficiently stable to be likely to have blood glucose concentrations 40 to 400 mg/dl, which is the range the CGMS can measure glucose concentrations. After clipping hair on the lateral thorax, the sensor was placed subcutaneously, and the monitor was attached using a cable. The monitor was then placed in

a harness that was attached to the cat.

Blood samples for measurement of glucose using a hand held glucometer were obtained every four hours beginning one hour after sensor placement for the duration of CGMS monitoring. Four of the blood glucose concentrations were required for calibration of the CGMS during a given 24 hour period, while the additional measurements on the glucometer were used for comparison with interstitial fluid values obtained from the CGMS. Glucose tracings were downloaded at least every 24 hours which is the maximum duration that the monitor can store data.

Results: All 14 cats tolerated the device well. Tracings of interstitial glucose concentrations were obtained in 15 of 16 attempts. Correlation of interstitial glucose with blood glucose concentrations was high. The sensor had to be replaced during recording in three patients, due to kinking of the sensor in two cases and removal by the cat in the other. Replacement of the sensor allowed measurements to continue successfully.

Seven of the 16 tracings were affected by the relatively narrow range of glucose concentrations measured by the CGMS. Hypoglycemia outside the measurable range (less than 40 mg/dl) was found in two cats, hyperglycemia above the measurable range in three cats, while one cat experienced both extremes of glucose. Marked variability in blood glucose concentrations from day to day was noted in three of eight cases where recordings were obtained for two or more days in a row despite the lack of changes in treatment and environment.

Conclusions: The CGMS is an accurate method of monitoring the response to insulin therapy in diabetic cats, but it should be

combined with other findings when making a change in treatment.

CLINICAL IMPACT:

Continuous glucose monitoring may be a useful and practical tool in some practices for monitoring glucose concentrations in diabetic cats. This monitor has previously been described to be used for glucose monitoring in the hospital and home environment in both dogs and cats. If used at home, the owner would have to measure the blood glucose concentration on at least three occasions over a 24 hour period in order to calibrate the monitor. Cost of equipment is a limitation, as the monitor is approximately \$2,000, the Com station is \$800, and the sensors are \$35.

This study demonstrated that some cats have considerable variability in their response to an identical dose of insulin. So, results of a single 10–12 hour blood glucose curve should be interpreted along with information from history, physical examination, and possibly measurement of fructosamine rather than on the blood glucose concentrations alone. Use of the CGMS would be likely to be an improvement over standard glucose curves if the tracing were monitored for 24 hours or more.

Cost of equipment is a limitation



Streptozotocin Treatment of Insulinoma

Bell R, Mooney CT, Mansfield CS, et al. Treatment of insulinoma in a springer spaniel with streptozotocin. *J Sm Anim Pract* 2005;46:247-250.

► INTRODUCTION:

Background: Insulinomas are malignant tumors of the pancreatic islets in dogs. Metastasis has typically occurred by the time of clinical diagnosis. Palliative treatment includes a high protein, fat, and complex carbohydrate diet to which prednisone is added when diet alone is insufficient in managing hypoglycemia. When diet modification and prednisone is insufficient for glycemic control, diazoxide to inhibit insulin release or octreotide, another inhibitor of insulin secretion, can be considered.

Streptozotocin is an antibiotic chemotherapeutic which destroys beta cells of the pancreatic islets. It is used to treat metastatic insulinoma in humans, but its toxicity to the kidneys in dogs creates a very narrow margin of safety in treating insulinomas in dogs.

Objectives: The objective of this report was to describe the results of using streptozotocin to treat an insulinoma in a dog.

✕ SUMMARY:

Case Report: An 8-year-old, spayed female, springer spaniel was presented with a history of exercise intolerance. Laboratory findings included marked hypoglycemia and inappropriate, high serum insulin concentration. An exploratory laparotomy was performed for suspected insulinoma. A pancreatic tumor and numerous masses in the liver and mesenteric lymph nodes were observed and biopsied. The primary tumor was not debulked. The histologic diagnosis was pancreatic carcinoma (insulinoma) with metastasis.

Post-surgical treatment include intravenous dextrose and prednisolone. Six days after the laparotomy, streptozotocin was administered as a single intravenous dose of 500 mg/m². Streptozotocin administration

was preceded and followed by diuresis using saline and dextrose. Prednisolone, at a tapering dose, was continued for four weeks.

Metastasis was present in the liver and cervical spine three months after administered streptozotocin

Re-evaluations at 10, 23, and 30 days after administered streptozotocin revealed hyperglycemia and glucosuria which were controlled by insulin injections.

The dog was presented 111 days after streptozotocin administration with cervical pain and lethargy. Radiographs of the cervical spine revealed an increased opacity in the seventh cervical vertebra. No abnormalities were present in the cytological examination of the cerebrospinal fluid. Two days of rest did not alleviate the cervical pain and the dog was euthanized at the owner's request. Necropsy results confirmed that the lesion was a metastatic insulinoma.

Conclusions: Streptozotocin can be used safely in dogs to treat insulinoma.

🌀 CLINICAL IMPACT:

The authors of this study believe that streptozotocin can be used safely in dogs. In the dog of this report, it was effective in controlling hypoglycemia from hyperinsulinemia, but metastasis was present in the liver and cervical spine three months after administered streptozotocin. If a higher or additional dose had been used, the efficacy may have been better, but it is unknown if it still would have been safe. Pre-treatment and post-treatment diuresis, as used in this dog, may reduce the toxicity of streptozotocin.

The reason that streptozotocin has efficacy with reasonable safety when used in humans is that it is administered by selective pancreatic arterial infusion to maximize insulinoma cytotoxicity and minimize renal toxicity. The dog of this report was administered strepto-

zotocin intravenously, and the primary tumor was not debulked. Patients that are strong enough for an exploratory laparotomy should have primary tumor excision when an insulinoma is evident.



Adrenocortical Hormones Responses to ACTH Stimulation

Frank LA, Davis JA, Oliver JW. Serum concentrations of cortisol, sex hormones of adrenal origin, and adrenocortical steroid intermediates in healthy dogs following stimulation with two doses of cosyntropin. *Am J Vet Res* 2004;65:1631-1633.

► INTRODUCTION:

Background: The diagnosis of hyperadrenocorticism is often based on the response in serum cortisol concentration after adrenocorticotrophic hormone (ACTH) stimulation. Cosyntropin is a synthetic form of ACTH used for stimulation tests. More recently, atypical forms of hyperadrenocorticism have been described in which other steroid hormones are produced in excess rather than, or in addition to, cortisol. The optimum dosage of cosyntropin and time for peak response for steroid hormones other than cortisol is not known.

Objectives: The objective of this study was to compare the effects of two different doses of cosyntropin on the serum concentrations of a variety of steroid hormones.

✕ SUMMARY:

Methods: Ten, healthy, neutered dogs were randomly assigned to either a group administered cosyntropin at 5 µg/kg or a group receiving 250 µg/kg, intravenously (IV). A cross-over treatment was performed one to two weeks later. Serum was collected before and 30, 60, 90, and 120 minutes after cosyntropin administration. Serum was assayed for cortisol, androstenedione, progesterone, 17-hydroxyprogesterone, and estradiol concentrations.

Results: Serum cortisol, androstenedione, progesterone, and 17-hydroxyprogesterone peaked at 60 minutes using either cosyntropin dose and without a significant difference in concentrations stimulated by the two doses between 0 to 90 minutes. A significantly higher concentration of steroids were present in the serum at 120 minutes when 250 µg/kg was administered. No increase in serum estradiol was detected after cosyntropin administration.

diol was detected after cosyntropin administration.

Conclusions: Cosyntropin can produce maximum production of cortisol, adrenal sex hormones, and adrenocortical intermediate steroids at one hour after 5 µg/kg, IV.

An increase in serum estradiol does not occur from stimulating the adrenal cortex to produce steroids



CLINICAL IMPACT:

This study confirmed that cortisol precursors and adrenal androgens are produced at the same rate under stimulation by ACTH (cosyntropin). It was possible that precursors to cortisol could have reached their maximum serum concentration before cortisol peak concentration, but all reached their peak at one hour after cosyntropin administration. The higher dosage of cosyntropin (250 µg/kg) does not cause a higher peak concentration of adrenal steroids in circulation, but it does cause a longer stimulation effect, extending at least 120 minutes.

The adrenal cortex is not the primary origin of estradiol. Most estradiol, not produced by the ovary, is produced by the enzyme, aromatase, converting testosterone to estradiol at peripheral cells. Aromatase activity is not affected by ACTH. So, an increase in serum estradiol does not occur from stimulating the adrenal cortex to produce steroids.



Primary Hyperaldosteronism in Cats

Ash RA, Harvey AM, Tasker S. Primary hyperaldosteronism in the cat: a series of 13 cases. *J Fel Med Surg* 2005;7:173-182.

► INTRODUCTION:

Background: Primary hyperaldosteronism has been described in the cat from functional adrenocortical tumors that produce excessive aldosterone. Hallmarks of the disease are muscle weakness due to severe hypokalemia, hypertension sometimes resulting in visual impairment due to retinopathy, an adrenal mass, and hyporeninemic hyperaldosteronism. Aldosterone secretion is stimulated primarily through activation of the renin-angiotensin system in response to hypovolemia and hypotension. Therefore, elevated plasma renin would be expected in a physiologic response that results in elevated plasma aldosterone. Primary hyperaldosteronism is diagnosed when plasma aldosterone is elevated in the presence of decreased plasma renin.

Objectives: The objectives of this retrospective study were to describe the clinical findings and response to treatment of cats with primary hyperaldosteronism.

✕ SUMMARY:

Methods: Records of cats with a diagnosis of hyperaldosteronism from two practices were reviewed. The diagnosis was based on finding hypertension or hyperkalemia, elevated plasma aldosterone concentration, and an adrenal mass.

Results: The 13 cats identified were primarily domestic short hair cats, with a range of age from 6 to 13 years. Eleven cats were presented with a primary complaint of muscle weakness that was acute in onset and severe in six of the cases. Manifestations of polymyopathy, including cervical ventroflexion, episodic weakness or stiffness, pain, dysphagia, and hind limb weakness or paresis, were reported

in 11 cats. Two cats presented because of acute onset of blindness. Both of these cats had intraocular hemorrhage and retinal detachment. Three other cats were noted to have hypertensive retinopathy.

Polyuria and polydipsia were noted in three cases. Polyphagia was present in two cats. Systolic blood pressure was elevated (more than 170 mmHg) in 11 of the 12 cats in which it was measured. Hypokalemia was found in all cats on initial evaluation, with plasma potassium less than 2.5 mEq/L in eight cats. Other biochemical abnormalities included elevated creatinine kinase in 10 of 11, elevated blood urea nitrogen in seven of 13, elevated creatinine in three of 13, and elevated T_4 in one of nine cases. The mean and range of urine specific gravities (9 cats) were 1.029 and 1.010 to 1.040, respectively.

Plasma aldosterone concentration was elevated in all cases. Abdominal ultrasound examination revealed a unilateral adrenal mass in all 11 cases so evaluated. Bilateral adenomas were noted on necropsy examination in two cats, one of which had a unilateral mass noted on ultrasound.

Treatment consisted of oral potassium gluconate and spironolactone in all cases. Amlodipine was administered to eight cats for treatment of hypertension. Intravenous fluids with potassium supplementation were administered to four cats. Treatment increased the potassium concentration in all cases, but it did not return to normal in any cat despite resolution of clinical signs of polymyopathy in all cases. Hypertension resolved during treatment in nine of 11 cases. Blindness persisted in the two cats presented with this problem.

Unilateral adrenalectomy, attempted in 10 cases, was successful in 7. Three cats

were euthanized because of intraoperative or immediate postoperative hemorrhage. Plasma aldosterone was below the reference range in five of the six cases where it was measured postoperatively and normal in the remaining case. Both cats treated only medically were euthanized due to chronic renal failure 304 and 984 days after diagnosis. Of the seven cases that survived the immediate postoperative period, one died due to sepsis 14 days after surgery and one was euthanized nearly three years after presentation due to a cranial abdominal mass of undetermined origin. The remaining five cats that had an adrenalectomy were alive 240 to 1803 days after presentation. A diagnosis of unilateral adrenal adenoma, unilateral adrenal adenocarcinoma, and bilateral adrenal adenoma was made in five, six, and two cases, respectively.

Conclusions: Primary hyperaldosteronism is not a rare disease and should be considered as a diagnosis in any cat with unexplained hypertension or hypokalemia.



CLINICAL IMPACT:

Although plasma renin was not measured in any of the cases in this report, the finding of hypokalemia, hypertension, and hyperaldosteronism in a cat with an adrenal gland mass is sufficiently definitive for a diagnosis of primary hyperaldosteronism. Although other causes of primary hyperaldosteronism causing bilateral adrenocortical hyperplasia occur in humans, these have not been documented in cats. It may be difficult to differentiate the hypokalemia and hypertension sometimes seen in cats with chronic renal failure from primary hyperaldosteronism without an abdominal ultrasound. Measurement of serum aldosterone is readily available from several veterinary diagnostic laboratories, but measurement of renin activity is not.

Primary hyperaldosteronism should be considered in any cat with unexplained hypertension or hypokalemia



Corticosterone- and Aldosterone-Secreting Tumor

Behrend EN, Weigand CM, Whitley EM, et al. Corticosterone- and aldosterone-secreting adrenocortical tumor in a dog. *J Am Vet Med Assoc* 2005;226:1662-1666.

► INTRODUCTION:

Background: Cortisol secreting adrenal tumors are the cause of 15-20% of hyperadrenocorticism in dogs. Recently, a small number of dogs with clinical signs of hyperadrenocorticism have been described to have excessive production of sex hormones. Aldosterone secreting tumors are rarely recognized in dogs and are expected to result in hypertension, hypokalemia, and metabolic alkalosis. Corticosterone is a steroid that is a precursor of aldosterone in its biosynthesis pathway. The diagnosis of a noncortisol secreting adrenal tumor can be difficult because the adrenocorticotrophic hormone (ACTH) response and low-dose dexamethasone suppression test results are not consistent with typical hyperadrenocorticism.

Objectives: The objective of this report is to describe a dog with an adrenal mass causing and increase in corticosterone and aldosterone secretion.

✕ SUMMARY:

Case Report: An 11-year-old, spayed female, Doberman pinscher was evaluated for suspected hyperadrenocorticism because of a three month duration of weakness, polyuria, polydipsia, enlarged abdomen, bilateral symmetrical alopecia, hyposthenuria, and elevated serum alkaline phosphatase activity. Examination revealed, in addition to the historical findings, a weak dog that was unable to rise without assistance, cervical ventroflexion, ataxia, hyporeflexia. Biochemical abnormalities in addition to those compatible with hyperadrenocorticism included hypokalemia (potassium 2.7 mEq/L), hypernatremia, and hyperchloremia. Treatment consisted of intravenous lactated Ringer's solution with supplemental potassium chloride as well as oral potassium gluconate. Muscle weakness resolved once the serum potassium concentration increased.

An enlarged right adrenal gland with

possible invasion of the caudal vena cava was noted on abdominal ultrasound. Results of an ACTH response test revealed normal basal plasma cortisol concentration with a suppressed response to stimulation. Plasma endogenous ACTH concentration was below the reference range and results of a high-dose dexamethasone suppression test showed lack of suppression of plasma cortisol, both consistent with hyperadrenocorticism due to a functional adrenal tumor.

Because of the hypokalemia and the presence of an adrenal gland mass, serum aldosterone was measured and found to be elevated before and after ACTH administration. An abdominal computed tomography examination revealed a right adrenal mass with invasion into the caudal vena cava. An adrenal adenocarcinoma was diagnosed by histopathology of biopsies obtained percutaneously with ultrasound guidance.

Because of clinical findings supportive of glucocorticoid excess, serum corticosterone was measured before and after another ACTH response test. The basal and post-ACTH plasma corticosterone concentrations were elevated, but the plasma cortisol concentration after ACTH was still below normal.

Mitotane was administered at a high dose (37.5 mg/kg, every 6 hours) along with prednisone (0.5 mg/kg daily) and potassium gluconate. After 14 days of treatment, water consumption was normal, serum sodium was slightly elevated, and serum potassium was normal. The adrenal mass decreased in size based on abdominal ultrasound examination. Basal and post-ACTH plasma aldosterone concentrations were suppressed, but cortisol and corticosterone were not measured. Mitotane, prednisone, and potassium gluconate were continued, and the dog returned nine days later with a history of occasional vomiting. Plasma aldosterone concentrations were still suppressed, potassium was normal, and the adrenal mass had further decreased in size. Potassium supplementation was dis-

The hallmarks of hyperaldosteronism are hypertension, hypokalemia, and metabolic alkalosis

continued, but the other medications were continued.

After an additional 12 days of treatment, results of the serum electrolytes and aldosterone concentrations were essentially unchanged. However, the adrenal mass was slightly smaller than on the previous examination. The dosage of mitotane was then reduced to 50 mg/kg three times per week. Calcinosis cutis and pyoderma were noted 49 days after initiating mitotane and prednisone treatment. Treatment with mitotane and prednisone were continued as previously, and antimicrobial treatment for the pyoderma was instituted. The dog was evaluated again 129 days after initial presentation because of acute tetraparesis, presumably the result of a cervical spinal cord lesion. The dog was euthanized, and necropsy was not performed.

Conclusions: This is the first description of an adrenal tumor producing both mineralocorticoids and glucocorticoids in the dog.

🌿 CLINICAL IMPACT:

The hallmarks of hyperaldosteronism are hypertension, hypokalemia, and metabolic alkalosis. Unfortunately, blood pressure was not evaluated in this case despite the high incidence of hypertension in both hyperaldosteronism and hyperadrenocorticism. While 40 to 50% of dogs with hyperadrenocorticism due to an adrenal tumor to have a normal plasma cortisol response to ACTH administration, it is unusual to have a subnormal increase in cortisol after ACTH. In this situation, measurement of other adrenal steroid hormones such as corticosterone, androstenedione, progesterone, or 17-hydroxyprogesterone might prove useful as was corticosterone in this case.



Hyperaldosteronism and Hyperprogesteronism

DeClue AM, Breshears LA, Pardo ID, et al. Hyperaldosteronism and hyperprogesteronism in a cat with an adrenal cortical carcinoma. J Vet Intern Med 2005;19:355-358.

► INTRODUCTION:

Background: Hyperadrenocorticism in cats is typically associated with hypercortisolemia. Adrenal tumors, particularly carcinomas, can cause atypical hyperadrenocorticism since the anaplasia that results in adrenocortical cells can promote or disrupt steroidogenesis enzymes in a variety of ways. Some adrenal carcinomas alter steroid production toward a predominance of progesterone, aldosterone, or adrenal androgens, or a varied combination of these.

Objectives: The reason for this report was to describe a cat with hyperaldosteronism and hyperprogesteronism from an adrenal cortical carcinoma.

✦ SUMMARY:

Case Report: A 12-year-old, castrated male, domestic long-haired cat was presented with a history of recent weight loss and an abdominal mass. Three months previously the cat was diagnosed with diabetes mellitus and treatment was begun with insulin.

Physical examination revealed partial alopecia, greasy hair, thin skin, a grade III/VI systolic murmur, and a cranial abdominal mass. Abnormal laboratory findings included marked hyperglycemia (460 mg/dl), azotemia (76 mg/dl), hypercreatinemia (3.1 mg/dl), and hypokalemia (3.5 mmol/L). Mild hypochloremia, hyperphosphatemia, and metabolic alkalosis were also present. Abdominal radiography and ultrasonography detected a mass cranial to the right kidney.

An adrenal tumor was suspected. Results of a low-dose dexamethasone suppression test (0.01 mg/kg, intravenously) were within normal limits. Serum aldosterone concentration was markedly elevated (more than 3,329 pmol/L, normal range: 94-388 pmol/L). Adrenocorticotrophic hormone (ACTH) stim-

ulation testing revealed higher than normal serum progesterone concentrations before and after ACTH, lower than normal serum cortisol concentrations before and after ACTH, and no increases after ACTH in serum testosterone, androstenedione, estradiol, or 17-hydroxyprogesterone concentrations.

Prior to laparotomy, potassium supplements were administered to no avail. During surgery, a 1.5 X 2.0 cm mass cranial to the right kidney was found associated with the vena cava. The left adrenal gland was grossly normal.

Histopathologic examination of the removed adrenal gland was consistent with an adrenocortical carcinoma. Serum aldosterone concentration was below normal range within two days after surgery. Postoperative complications ensued and death occurred after three days of intensive care. Necropsy was not permitted.

Conclusions: The diabetic cat of this report had an adrenocortical carcinoma that produced excessive aldosterone and progesterone.

🌀 CLINICAL IMPACT:

The degree of excess aldosterone production (and its precursor, progesterone) in this cat was massive. An inability to sufficiently replace potassium before the tumor excision is not surprising since aldosterone would have caused continual, severe kaliuresis. A cranial abdominal mass concurrent with hypokalemia is a cardinal sign of an aldosteronoma.

A cranial abdominal mass concurrent with hypokalemia is a cardinal sign of an aldosteronoma



Mitotane and Bone Marrow Necrosis

Weiss DJ. Bone marrow necrosis in dogs: 34 cases (1996-2004). *J Am Vet Med Assoc* 2005;227:263-267.

► INTRODUCTION:

Background: Bone marrow has a high mitotic index and is particularly susceptible to damage from ischemia and toxins. Nonregenerative anemia, leukopenia, or thrombocytopenia can result from bone marrow necrosis. Some of the potential known causes include drugs, parvovirus, monocytic ehrlichiosis, septicemia, endotoxemia, and malignancy.

Objectives: The objective of this study was to identify the causes and clinical and laboratory findings of bone marrow necrosis in dogs.

✦ SUMMARY:

Methods: The results of 609 cytologic bone marrow evaluations and the medical records of 34 dogs (5.6% of samples examined) diagnosed with bone marrow necrosis were reviewed.

Results: Among 34 dogs with bone marrow necrosis, nine had no identifiable cause while 25 had associated disease or drug administration. All dogs with idiopathic bone marrow necrosis had myelofibrosis and anemia, three also had neutropenia, and three also had thrombocytopenia. Of the 25 others, 14 (56%) had anemia, 14 (56%) had neutropenia, and 18 (72%) had thrombocytopenia. Ten (40%) had myelofibrosis.

Diseases associated with bone marrow necrosis were primarily sepsis, lymphosarcoma, and systemic lupus erythematosus. Drug administration associated with bone marrow necrosis included chemotherapeutics (cyclophosphamide or vincristine), colchicine, phenobarbital, carprofen, metronidazole, fenbendazole, and mitotane.

Conclusions: Bone marrow necrosis is a significant cause for hematologic disorders in dogs. An associated disease or drug administration can be identified in most cases.

🌀 CLINICAL IMPACT:

Two of the 34 dogs with bone marrow necrosis had been administered mitotane. Mitotane is not a known bone marrow toxin, and a cause-effect relationship was not established. However, dogs under treatment for hyperadrenocorticism could have reasons for bone marrow necrosis related to the disease, rather than the drug used for treatment. Hyperadrenocorticism can lead to thromboembolism, sepsis, and hepatopathy which can cause bone marrow necrosis. Hyperestrogenism which can be associated with hyperadrenocorticism is a well known cause bone marrow aplasia in dogs. The risk of bone marrow necrosis is probably greater from not controlling hyperadrenocorticism than it is from the use of mitotane.

The risk of bone marrow necrosis is probably greater from not controlling hyperadrenocorticism than it is from the use of mitotane



Glucocorticoid-Induced Urinary Tract Infection

Torres SMF, Diaz SF, Nogueira SA, et al. Frequency of urinary tract infection among dogs with pruritic disorders receiving long-term glucocorticoid treatment. *J Am Vet Med Assoc* 2005;227:239-243.

► INTRODUCTION:

Background: Glucocorticoid excess, whether due to exogenous administration or spontaneous hyperadrenocorticism, causes immunosuppression. This is most frequently manifested as urinary tract infections (UTI) which are often asymptomatic. In addition, evidence of inflammation has been reported to be absent in many cases of UTI due to glucocorticoid excess, making a diagnosis of infection dependent on urine culture. The evidence supporting frequent infection in dogs administered glucocorticoids has been derived from a single study.

Objectives: The objectives of this investigation were to determine if the frequency of UTI in pruritic dogs administered glucocorticoids is greater than that in pruritic dogs not administered a glucocorticoid, to determine if urinalysis is an adequate screening test for UTI, and if the dosage, type, or duration of glucocorticoid treatment is associated with development of a UTI.

✦ SUMMARY:

Methods: Medical records of dogs evaluated for pruritus that had received glucocorticoids for at least six months and had a urine sample obtained by cystocentesis submitted for bacterial culture were reviewed. The controls for this case-control study were enrolled prospectively by evaluating urinalysis and urine culture in dogs evaluated for pruritus that had not received topical or systemic glucocorticoids during the preceding six months and had never received glucocorticoids for more than four weeks at any given time.

One hundred twenty-seven dogs that received glucocorticoid treatment and 94 control dogs that had not received glucocorticoids were included in the study. Most dogs

in both groups had atopy as the underlying cause of pruritus. Prednisolone was administered to 70% and methylprednisolone to 30% of the dogs receiving glucocorticoids. The glucocorticoid dosage ranged from 0.12 to 1.0 mg/kg (mean, 0.28 mg/kg) every 48 hours. All but two dogs had been administered a dose less than 1 mg/kg every other day and four dogs received glucocorticoids every 24 hours. The duration of treatment was 6.7 months to 7 years.

A single urine sample was submitted in 57 dogs, two samples were submitted in 46 dogs, and three samples were submitted in 11 dogs, and four or more samples were submitted in 13 dogs administered glucocorticoids. A single urine sample was analyzed in all the controls. Urine was collected while dogs were receiving antimicrobial treatment in 59 of the 240 urine samples in the glucocorticoid treatment group. Nine of the 94 control dogs were on antimicrobial treatment at the time of urine collection.

Results: Clinical signs of urinary tract infection were not reported by owners of any of the dogs studied. A positive urine culture was obtained in at least one sample in 23 of the 127 dogs receiving glucocorticoids and in none of the control dogs. Of the 23 dogs with positive urine cultures, multiple samples were collected from 18. Six of the 18 dogs had positive cultures on an additional sample. Ten different bacterial species were isolated, and five samples contained two isolates. *Escherichia coli* was cultured in 14 samples; *Enterococcus* species was found in six samples. Six positive cultures were obtained from dogs that were receiving an antimicrobial (cephalexin in all cases). Female dogs were significantly more likely to have a UTI than males. The type, dose, and duration of glucocorticoid administration was not significantly associated with urinary tract infection.

Bacteriuria or pyuria was identified in 22 and 15, respectively, of the 29 the urinalyses of dogs with positive urine cultures.

Conclusions: Dogs receiving glucocorticoids for long periods of time are at risk for developing a UTI, and urine samples should routinely be cultured at least once per year from dogs being administered glucocorticoids.



CLINICAL IMPACT:

The finding of frequent UTI in this study of dogs receiving relatively small doses of glucocorticoid every other day confirms that periodic monitoring of urine cultures should be performed in dogs receiving long-term treatment. This is particularly important in dogs being treated for immune-mediated diseases that receive higher doses more frequently than do dogs treated for allergies. The lack of clinical signs of UTI and the frequent absence of pyuria or bacteriuria make history and urinalysis suboptimal methods of monitoring for the presence of a UTI in dogs treated with glucocorticoids. While the consequences of subclinical urinary tract infections in this population remains to be determined, it seems prudent to treat the infection as it is diagnosed.

Periodic monitoring of urine cultures should be performed in dogs receiving long-term glucocorticoid treatment



Ovariohysterectomy and Risk of Feline Mammary Carcinoma

Overley B, Shofer FS, Goldschmidt MH, et al. Association between ovariohysterectomy and feline mammary carcinoma. *J Vet Intern Med* 2005;19:560-563.

► INTRODUCTION:

Background: Approximately half of mammary gland tumors in dogs are malignant and at the time of diagnosis about half of malignant mammary tumors have metastasized. In contrast, 90% of mammary tumors in cats are adenocarcinomas which have generally metastasized prior to presentation for treatment.

The risk of mammary cancer is nearly eliminated in dogs if they are spayed prior to their first estrus period. If not spayed until after 2.5 years of age, no reduction in risk is believed to occur. The degree of beneficial effects on the risk of mammary cancer of spaying cats while they are young is not known although estrogens or progestins, or both, are assumed to play a causative or enhancing role in the development of feline mammary cancer.

Objectives: The purpose of this study was to evaluate the influence of age when spayed, pregnancies, and progestin exposure on the incidence of mammary carcinoma in cats.

✦ SUMMARY:

Methods: Questionnaires were sent to veterinarians who cared for 308 female cats that had a histologic diagnosis of mammary carcinoma and 400 female cats that had a mammary biopsy but without histologic evidence of mammary carcinoma. Cats with mammary carcinoma and cats that were controls were frequency matched for age and year of diagnosis. The questionnaire was designed to collect data on the effect that age when spayed, the breed, progestin exposure, and pregnancies had mammary gland carcinoma development.

Results: The overall response to the request to complete and return the questionnaires was 58%. Intact (not spayed) cats had a

significantly higher risk for mammary gland carcinoma. The risk of mammary carcinoma development was reduced 91% if spayed before six months of age and 86% if spayed before a year of age. Pregnancies had no effect on the risk of mammary carcinoma. There were insufficient cases with progestin exposure to determine the effect on risk of neoplasia of the mammary glands.

Conclusions: Cats that are spayed prior to a year of age have significantly reduced risk of developing mammary gland carcinoma.

🌀 CLINICAL IMPACT:

Mammary gland tumors are the third most often diagnosed neoplasm in female cats. The prognosis for the vast majority is extremely poor. Survival rates are usually less than a year. Neither early detection and excision nor medical management are highly effective means of preventing deaths from mammary carcinoma in older female cats, but early spaying is. Spaying female cats prior to six months of age can easily, humanely, and economically spare the lives of 90% of the cats otherwise at risk for malignant mammary tumors.

Spaying female cats prior to six months of age can spare the lives of 90% of the cats otherwise at risk

Thyro-Tabs[®]

(levothyroxine sodium tablets, USP)

Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

Description:

Each Thyro-Tabs[®] tablet provides synthetic crystalline levothyroxine sodium (L-thyroxine).

Indications:

For use in dogs for correction of conditions associated with low circulating thyroid hormone (hypothyroidism). Low serum circulating T-4 concentrations, coupled with clinical signs, are suggestive of hypothyroidism. The following T-4 concentrations in canine serum have been established:

Normal (euthyroid) – 18 to 32 ng/mL (18 to 32 µg/dL)

Possible hypothyroid - 10 to 18 ng/mL (10 to 18 µg/dL)

Hypothyroid – less than 10 ng/mL (10 µg/dL)

Hypothyroidism is unlikely with a resting serum T-4 concentration of 18 ng/mL or above. A dog exhibiting signs of hypothyroidism with a T-4 below 18 ng/mL should be considered for levothyroxine replacement therapy. Confirmation of the diagnosis could include withdrawal of therapy after which a recurrence of clinical signs further supports the diagnosis. Correct diagnosis of hypothyroidism is important, since such a diagnosis normally commits an animal to life-long replacement therapy. The principle objective of levothyroxine sodium administration is to achieve and maintain normal metabolism in the animal's normal physiologic range. Animal adaptation may necessitate regular monitoring of serum T-4 concentrations during the first several months of treatment to establish maintenance doses. TSH testing may be used to provide a definitive diagnosis in dogs with borderline resting T-4 values.

Mode of actions:

Levothyroxine sodium provided by Thyro-Tabs cannot be distinguished from that endogenously secreted by the thyroid gland. The primary regulator of thyroid function is thyroid stimulating hormone (TSH) which is synthesized and secreted by the pars distalis of the adenohypophysis (anterior pituitary). The mediator from the hypothalamus which exerts a continuous influence over the release of TSH is

thyrotropin-releasing hormone (TRH).

Hypothyroidism in the dog:

Hypothyroidism usually occurs in older and middle-aged dogs although the condition will sometimes be seen in younger dogs of the larger breeds. Neutered animals of either sex are also frequently affected, regardless of age. The condition is primary failure of the thyroid gland because of lymphocytic thyroiditis or other loss of follicular epithelium and resulting atrophy of the gland. Secondary hypothyroidism is rare and usually due to a destructive pituitary tumor.

Clinical signs:

The following list of clinical signs and laboratory findings may vary depending upon the degree of thyroid dysfunction:

Nerve and muscle function: lethargy, lack of endurance, increased sleeping, reduced alertness and interest with dulled mental attitude, hypotonus, stiff, slow movements, dragging of forelimbs, head tilt, disturbed balance, unilateral facial paralysis.

Metabolism: decreased oxygen consumption and lower metabolic rate, sensitivity and intolerance to cold, low body temperature, cool skin, heat seeking, increased body weight, constipation, poor exercise tolerance, slow heart rate, weak pulse, weak apex heart beat and low voltage on ECG.

Reproduction: reproductive failure, abortion, stillbirth, live birth of weak young, delayed puberty, reduced libido, impaired spermatogenesis, irregular estrus and anestrus, galactorrhea.

Skin and hair: myxedema of the face, blepharoptosis, atrophy of epidermis, thickening of the dermis, surface and follicular hyperkeratosis, hyperpigmentation, coarse and sparse coat, dry, dull and brittle hair, slow regrowth and retarded turnover of hair and bilateral alopecia.

Laboratory findings: low serum T-4 concentrations, hypercholesterolemia, hypertriglyceridemia, elevated serum creatine kinase, normochromic, normocytic anemia.

Contraindications:

Therapy is contraindicated in thyrotoxicosis, acute myocardial infarction, and uncorrected adrenal insufficiency. Other conditions in which the use of therapy should be used with caution include primary hypertension, euthyroidism, and pregnancy.

Precautions:

The administration of levothyroxine sodium to dogs to be used for breeding purposes or in pregnant bitches has not been evaluated. There is evidence that administration to pregnant bitches may affect the normal development of the thyroid gland in the unborn pups. The clinical effects of therapy are slow in being manifested. Overdosage may produce the signs of thyrotoxicosis including but not limited to: polydipsia, polyuria, polyphagia, reduced heat tolerance and hyperactivity or personality change. Thyro-Tabs 0.1 mg and 0.7 mg tablets contain FD&C yellow #5 (tartrazine) which has been associated with allergic-type reactions (including bronchial asthma) in susceptible humans. It is unknown if such a reaction could also occur in dogs.

Adverse reactions:

There are no specific adverse reactions associated with therapy at the recommended dosages. Overdosage will result in thyrotoxicosis.

Dosages:

The initial recommended daily dose is 0.1 to 0.2 mg/10 pounds (4.5 kg) body weight in single or divided doses. Dosage is adjusted by monitoring T-4 blood levels of the dog every four weeks until an adequate maintenance dose is established. The usual daily maintenance dose is 0.1 mg/10 pounds (4.5kg). A maximum of 0.8 to 1.0 mg total daily dose will be sufficient in many dogs over 80 pounds in body weight.

Administration:

Thyro-Tabs may be administered orally or placed in the food.

How supplied:

Available as scored, color-coded caplets in 9 concentrations: 0.1 mg, 0.2 mg, 0.3 mg, 0.4 mg, 0.5 mg, 0.6 mg, 0.7 mg, 0.8 mg and 1.0 mg in 28 tablet strip packs, bottles of 120 and 1,000.

Storage:

Store at controlled room temperature; 15°-30°C (59°-86°F) and protect from light.

References: See package insert.



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Journals examined by the editors for article inclusion:

American Journal of Veterinary Research	Journal of Veterinary Medical Science
Australian Veterinary Journal	Journal of Veterinary Medicine, Series A
Canadian Journal of Veterinary Research	Journal of Comparative Pathology
Canadian Veterinary Journal	Journal of Veterinary Pharmacology and Therapeutics
Domestic Animal Endocrinology Endocrinology	New Zealand Veterinary Journal
European Journal of Endocrinology	Research in Veterinary Science
Journal of Veterinary Internal Medicine	Veterinary Journal
Journal of the American Animal Hospital Association	Veterinary Pathology
Journal of Small Animal Practice	Veterinary Record
Journal of the American Veterinary Medical Association	Veterinary Radiology & Ultrasound
Journal of Veterinary Diagnostic Investigationand more than 20 others

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