

Endocrinology

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

IN THIS ISSUE

- 1 Hypophyseal Evaluations**
 - Dynamic Computed Tomography of the Pituitary
 - Vasopressin Response to Osmotic Stimulation in Dogs with Polyuria and Polydipsia
- 4 Hypothalamic-Hypophyseal Disorders**
 - Traumatic Partial Hypopituitarism
- 5 Tests of Thyroid Function**
 - Diagnostic Value of Endogenous Canine TSH in the Diagnosis of Hypothyroidism
 - Tryptic Peptides of Canine Thyroglobulin and Autoimmune Thyroiditis
- 7 Hyperthyroidism**
 - Transdermal Methimazole for the Treatment of Feline Hyperthyroidism
- 8 Hypercalcemia**
 - Serum 25-Hydroxycholecalciferol and 1,25-Dihydroxycholecalciferol in Dogs
- 9 Diabetes Mellitus**
 - Plasma-Ionized Magnesium Concentration in Dogs with Diabetes Mellitus
 - Hyperglycemic, Hyperosmolar Syndrome in Feline Diabetics
 - Funduscopic Findings Following Phacoemulsification in Diabetic Dogs
- 12 Pancreatic Islet Tumors**
 - Canine Gastrinoma
- 13 Adrenal Function Testing**
 - Adrenal Steroid Hormone Concentrations in Dogs with Alopecia X
 - Otic Glucocorticoids and Adrenal Function.
 - Plasma Renin Activity, Adrenocortical Hormones, and α -Melanocyte-Stimulating Hormone in Cats
 - Urinary Corticoid:Creatinine Ratios After Oral Low-Dose Dexamethasone Suppression
- 17 Hyperadrenocorticism**
 - Treatment of Canine Alopecia X with Trilostane
 - Indicators of Canine Adrenocortical Tumor Malignancy
 - Effect of Trilostane on Serum Aldosterone, Cortisol, and Potassium Concentrations in Dogs with Hyperadrenocorticism
- 20 Gonadal Disorders**
 - Persistent Mullerian Duct Syndrome Causing Male Pseudohermaphroditism



Dynamic Computed Tomography of the Pituitary

van der Vlugt-Meijer RH, Meij BP, Voorhout G. Dynamic computed tomographic evaluation of the pituitary gland in healthy dogs. Am J Vet Res 2004;65:1518-1524.

► INTRODUCTION:

Background: Approximately 85% of spontaneous cases of hyperadrenocorticism in dogs are pituitary-dependent. Most of these are caused by microadenomas of the pituitary which may not be visible on computed tomography (CT) scan of the pituitary due to their small size and similar consistency (isoattenuation) to the surrounding pituitary tissue. Dynamic contrast-enhanced CT is a series of image slices through the pituitary during and after the intravenous (IV) injection of a contrast medium. In humans, the medium first enhances the central part of the secondary capillary bed of the adenohypophysis (the pituitary tuft) followed by the centrifugal enhancement of pars distalis. Microadenomas can cause alteration of the tuft.

Objectives: The purpose of this study was to determine the pattern of contrast enhancement produced by dynamic CT of the pituitary in healthy dogs.

✕ SUMMARY:

Methods: Seventeen healthy dogs were given general anesthesia and examined by dynamic contrast-enhanced CT of the pituitary. Nine to 11 transverse scans were made perpendicular to the skull base during and after the IV injection of an iodine-containing contrast medium.

Results: The contrast medium sequentially enhanced the maxillary arteries, internal carotid arteries, and arterial cerebral circle. The central part of the pituitary was strongly enhanced followed by central clearing with enhancement of the periphery of the pituitary.

Conclusions: The central enhancement by contrast media was attributed to direct arterial vascularization of the neurohypophysis.

Peripheral enhancement was from venous vascularization of the pars distalis. Distortion or displacement of the central enhancement was believed potentially useful for detecting microadenomas in the pars distalis.

Dynamic imaging of the pituitary in dogs may disclose occult microadenomas.



CLINICAL IMPACT:

Although dynamic CT vascular patterns of the pituitary are similar between humans and dogs, the reasons differ. Central filling in humans is due to the pituitary tuft. In dogs, it is the filling of the arterial supply to the neurohypophysis. The authors speculate that dynamic imaging of the pituitary in dogs may disclose occult microadenomas. However, the sensitivity of detection may be less than in humans since the pituitary tuft should be more easily distorted or compressed by an adjacent microadenoma than would be the arterial supply to the neurohypophysis by an adjacent microadenoma.

- ▶ Pituitary microadenomas may be best imaged by alterations in the “pituitary flush” from intravenous injection of contrast media during CT scanning. *Am J Vet Res* 2004;65:1518-1524.
- ▶ Vasopressin response to hypertonic saline infusion is not the ideal means of differentiating the causes of polyuria and polydipsia in dogs. *J Vet Intern Med* 2004;18:800-806.
- ▶ Post-traumatic diabetes insipidus has been described in a cat. *J Sm Anim Pract* 2004;45:405-409.
- ▶ The canine-TSH assay has high specificity but low sensitivity and cannot reliably exclude the diagnosis of primary hypothyroidism. *Schweiz Arch Tierheilk* 2004;146:183-188.
- ▶ Autoimmune thyroiditis may be detected by antibodies to tryptic peptides of thyroglobulin. *Vet Immunol Immunopathol* 2004;101:271-276.
- ▶ Transdermal methimazole is not as effective as oral methimazole within two weeks of starting treatment, but it is better tolerated. *J Vet Intern Med* 2004;18:651-655.
- ▶ Serum levels of 25-hydroxycholecalciferol and 1,25-dihydrocholecalciferol in dogs with hypercalcemia are variable and unpredictable. *Vet Res Commun* 2004;28:669-680.
- ▶ Hair regrowth in dogs with Alopecia X is not mediated by changes in adrenocortical steroid production. *Vet Dermatol* 2004;15:278-284.
- ▶ Adrenocortical suppression caused by two weeks of otic glucocorticoid administration can persist for two weeks after discontinuing treatment. *Vet Dermatol* 2004;15:363-368.
- ▶ Neutering or aging significantly alters plasma aldosterone-to-renin ratio in cats. *J Vet Intern Med* 2004;18:625-631.
- ▶ The lowest dose of oral dexamethasone that will reliably suppress urinary corticoid:creatinine ratio in healthy dogs is 0.01 mg/kg. *Vet Rec* 2004;155:518-521.
- ▶ Trilostane is an effective treatment for canine Alopecia X in at least 85% of cases. *Vet Dermatol* 2004;15:285-293.
- ▶ Adrenocortical adenomas and carcinomas are best differentiated by thorough evaluation of morphologic features and immunohistochemical assessment of the proliferation index. *Vet Pathol* 2004;41:490-497.
- ▶ Trilostane suppresses serum cortisol concentration in dogs more than it suppresses serum aldosterone concentration. *Am J Vet Res* 2004;65:1245-1250.
- ▶ Hypomagnesemia is not a typical finding in diabetic dogs at initial presentation for glycemic control treatment. *J Vet Intern Med* 2004;18:612-617.
- ▶ Diabetic cats with nonketotic hyperosmolar syndrome usually have concurrent renal failure or congestive heart failure. *J Vet Emerg Crit Care* 2004;14:30-40.
- ▶ Diabetic vasculopathy may be more common in diabetic dogs than previously believed. *J Am Vet Med Assoc* 2004;225:709-716.
- ▶ A dog has been reported with a gastrinoma that was associated with abdominal ultrasonographic changes. *J Vet Med Sci* 2004;66:993-995.
- ▶ Persistent Mullerian duct syndrome has been reported in a mixed-breed dog with pseudohermaphroditism. *Vet Rec* 2004;155:400-401.



Vasopressin Response to Osmotic Stimulation in Dogs with Polyuria and Polydipsia

van Vonderen IK, Kooistra HS, Timmermans-Sprang EPM, et al. Vasopressin response to osmotic stimulation in 18 young dogs with polyuria and polydipsia. *J Vet Intern Med* 2004;18:800-806.

► INTRODUCTION:

Background: Most disorders causing polyuria and polydipsia can be diagnosed using routine laboratory testing, so more sophisticated evaluations of urine concentrating ability or responsiveness are rarely needed. In those cases where the diagnosis is in question after routine testing, a water deprivation test or response to desmopressin administration are often utilized. The hypertonic saline infusion test is another method of evaluating factors involved in urine concentration, where plasma osmolality is gradually increased during intravenous (IV) infusion of 20% saline. Normally, small increases in plasma osmolality are associated with increased vasopressin (antidiuretic hormone) secretion. It may be possible to classify polyuric disorders based on the vasopressin response to elevated plasma osmolality.

Objectives: The objective of this study was to determine if the vasopressin response to elevated plasma osmolality is useful in evaluating young dogs with polyuria and polydipsia.

✕ SUMMARY:

Methods: The cause of polyuria and polydipsia was investigated in 18 dogs (13 male, five female) aged 3 to 32 months (median eight months) in which history, physical examination, and routine laboratory testing did not reveal a cause. Serial measurements of urine osmolality every two to four hours for 24 hours were obtained in 14 dogs with continuous access to water.

Seven dogs were then administered desmopressin every eight hours for four days and serial urine osmolality was repeated. Four other dogs had a urine osmolality measured only before and after desmopressin

administration, and an additional three dogs had urine osmolality measured in response to desmopressin at the end of a water deprivation test. The response to desmopressin was considered small, medium, or large if there was an increase in urine osmolality less than 25%, 25 to 75%, or more than 75%, respectively.

Measurement of vasopressin during hypertonic saline infusion may be of limited use in determining the cause of polyuria and polydipsia.

A water deprivation test was performed in all dogs. The final testing was with a hypertonic saline infusion, where plasma vasopressin concentration and osmolality were measured in response to IV infusion of 20% NaCl at 0.03 ml/kg/min for two hours. These measures were used to estimate the sensitivity of the osmoregulatory system and the threshold osmolality at which vasopressin secretion is stimulated. Dogs were classified as having an exaggerated vasopressin response, a subnormal vasopressin response, or a nonlinear vasopressin response to increased plasma osmolality.

Results: An exaggerated vasopressin response to hypertonic saline infusion was found in three dogs. The osmotic threshold for vasopressin secretion was increased in one and normal in two of these dogs. Urine osmolality while dogs had access to water ranged from 823 to 1658 mOsm/kg and exceeded 1000 mOsm/kg during water deprivation testing in two of the three dogs with an exaggerated vasopressin response.

The response to desmopressin was large in one dog and small in the other dog tested. A subnormal vasopressin response to hypertonic saline infusion was found in four dogs. The osmotic threshold for vasopressin release was increased in three dogs and the sensitivity of the vasopressin response was decreased in one. The maximum urine osmolality without challenge varied widely in this group. The

response to desmopressin was large in two, medium in one, and absent in one dog.

During the water deprivation test, urine concentration was low or moderate in three dogs and the urine osmolality nearly reached 1000 mOsm/kg in one dog in the subnormal vasopressin response group. There were 11 dogs that had a nonlinear vasopressin response, an abrupt increase in vasopressin that occurred unrelated to the gradual increase in plasma osmolality during hypertonic saline infusion. The osmotic threshold was increased in seven dogs and the sensitivity was decreased in 3. There was wide variability in the urine osmolality during serial collection and in response to desmopressin administration. Urine osmolality exceeded 1000 mOsm/kg in four dogs during water deprivation testing and in two dogs prior to water deprivation.

Conclusions: Measurement of vasopressin during hypertonic saline infusion is widely variable and may be of limited use in determining the cause of polyuria and polydipsia in dogs.



CLINICAL IMPACT:

This study highlights the difficulty in evaluating dogs with polyuria and polydipsia and demonstrated that categorization on the basis of vasopressin response to hypertonic saline was of little practical use. For example, based on ability to concentrate urine spontaneously or during a water deprivation test, nine dogs would have been classified as having primary polydipsia. These dogs were present in all three categories of vasopressin responsiveness. Because vasopressin secretion is episodic, the increases noted during hypertonic saline infusion may have occurred spontaneously and not in response to increased plasma osmolality.



Traumatic Partial Hypopituitarism

Smith JR, Ehwood CM. Traumatic partial hypopituitarism in a cat. *J Sm Anim Pract* 2004;45:405-409.

► INTRODUCTION:

Background: Cranial trauma can cause temporary or permanent, complete or partial hypopituitarism by hemorrhage, edema, or thrombosis or by shearing of the portal system of the median eminence of the ventral hypothalamus or the pars tuberalis (pituitary stalk).

Objectives: The purpose of this report was to describe the first reported case of partial hypopituitarism of the adenohypophysis and neurohypophysis caused by trauma in a cat.

✦ SUMMARY:

Case Report: An 11-month-old, castrated male cat with a history of having polyuria, polydipsia, lethargy, and irritability for three months was evaluated. Six weeks prior to presentation the cat had been hit by a motor vehicle causing mydriasis on the right side. Radiographs of the skull, thorax, and abdomen had findings within normal limits. Glucocorticoids were administered for three days. Follow up for four subsequent weeks revealed isosthenuria.

Neurological examination confirmed the presence of mydriasis on the right side, plus left foreleg tactile and visual placing responses. Proprioceptive deficits were present on the left side of the body. Pupillary light responses were sluggish on the right side. Polydipsia (mean water intake of 186 ml/kg/day) and low urine specific gravity (1.016) were noted.

Hypopituitarism was suspected. Basal serum cortisol concentration was low with normal adrenocorticotrophic hormone (ACTH) stimulation results. Endogenous ACTH concentration was normal. Serum T₄, thyroid-stimulating hormone (TSH), and insulin growth factor-I concentrations were low. Prednisolone was prescribed to treat secondary hypoadrenocorticism.

The cat's temperament improved during a four month period prior to re-examination. However, tactile and visual placing responses and proprioception remained deficient in the left foreleg. Free T₄ concentration was within normal range. Two water deprivation test results were consistent with a diagnosis of diabetes insipidus. Response to desmopressin administration was significant and indicated an endogenous antidiuretic hormone (ADH) deficiency, i.e. central (hypothalamic-neurohypophyseal) diabetes insipidus. Ocular administration of desmopressin, twice per day, was administered with good response and continued.

Conclusions: The cat in this report had post-traumatic hypopituitarism that included secondary hypoadrenocorticism and central diabetes insipidus.



CLINICAL IMPACT:

Severe head trauma in dogs and cats may be associated with transient or permanent polyuria and polydipsia due to central diabetes insipidus. Long-term re-evaluations are warranted since resolution of edema or thrombosis, or regeneration of hypothalamic-neurohypophyseal neurons can occur with a resumption of normal ADH synthesis and secretion eliminating the need for life-long treatment.

The sites of ADH synthesis, transport, and secretion are more resistant to trauma than is the vascular supply and tissue of the adenohypophysis. Most cases of post-traumatic hypopituitarism in dogs and cats probably go unrecognized clinically since gonadotropes and somatotropes are most susceptible to damage from trauma. Companion dogs and cats are usually neutered and have no adverse effects from growth hormone (GH) deficiency. The next most trauma-susceptible pituitary

cells are thyrotropes and then corticotropes. The cat in this report was neutered, so gonadotropin secretion was unassessed. It did have a deficiency of IGF-I (mediator of growth hormone effects), T₄, and cortisol as well as a deficiency of ADH.

Severe head trauma in dogs and cats may be associated with transient or permanent polyuria and polydipsia.



Diagnostic Value of Endogenous Canine TSH in the Diagnosis of Hypothyroidism

Foretti FS, Reusch CE. Endogenous TSH in the diagnosis of hypothyroidism in dogs. *Schweiz Arch Tierheilk* 2004;146:183-188.

► INTRODUCTION:

Background: A diagnosis of hypothyroidism should be based on appropriate thyroid function test results in a dog with clinical findings compatible with the disease. Lack of access to bovine thyroid-stimulating hormone (TSH) and high cost of human recombinant TSH has resulted in the TSH response test being restricted to use in a research setting. Without this test, widely considered the “gold standard” for diagnosis of hypothyroidism, confirming the diagnosis is typically dependent on measurement of serum concentrations of total thyroxine (T_4), free T_4 (fT_4) by equilibrium dialysis, and endogenous canine TSH. While elevated serum TSH concentration is a requisite for diagnosis of primary hypothyroidism in humans, measurement of TSH in dogs has been less rewarding. **Objectives:** The objective of this study was to evaluate the use of serum TSH concentrations in dogs suspected of having hypothyroidism.

Low sensitivity limits for the canine TSH assay does not allow it to be used to exclude a diagnosis of hypothyroidism.

✕ SUMMARY:

Methods: Serum total T_4 and endogenous TSH were measured in sera of 65 dogs with clinical signs consistent with hypothyroidism. Dogs were determined to be hypothyroid based primarily on results of a TSH response test. For this test, serum T_4 was measured before and six hours after intramuscular injection of bovine TSH at a dose of 1 unit for dogs less than 25 kg and 2 units for dogs 25 kg, or more. Dogs were considered euthyroid if the post-TSH T_4 concentration was more than 2.5 $\mu\text{g}/\text{dl}$ and there was an increase in T_4 of at least 1.5 times the basal concentration or if clinical signs resolved without thyroid hormone supplementation. Dogs were considered hypothyroid if the post-TSH T_4 concentration was less than 1.6 $\mu\text{g}/\text{dl}$ or less

than 1.5 times the baseline concentration.

Results: Hypothyroidism was diagnosed in 26 dogs. Post-TSH T_4 concentrations in hypothyroid dogs ranged from 0.1 to 3.4 $\mu\text{g}/\text{dl}$, with a median of 0.35 $\mu\text{g}/\text{dl}$.

Euthyroid dogs had post-TSH T_4 concentrations ranging from 1.7 to 7.3 $\mu\text{g}/\text{dl}$ with a median of 4.0 $\mu\text{g}/\text{dl}$. In the 26 hypothyroid dogs, basal serum T_4 concentration was less than 0.5 $\mu\text{g}/\text{dl}$ in 18, 0.5 to 1 $\mu\text{g}/\text{dl}$ in five, and 1.0 $\mu\text{g}/\text{dl}$, or more in 3. In euthyroid dogs, basal serum T_4 was less than 0.5 $\mu\text{g}/\text{dl}$ in one, 0.5-1.0 $\mu\text{g}/\text{dl}$ in four, 1.0 to 1.4 $\mu\text{g}/\text{dl}$ in 11, and 1.5 $\mu\text{g}/\text{dl}$, or more, in 23. Serum TSH was elevated (more than 0.6 ng/ml) in 15 of 26 hypothyroid dogs and was within the reference range in all euthyroid dogs, giving a sensitivity of 58% and a specificity of 100%. The sensitivity was increased to 73% and specificity remained at 100% if the upper limit of the reference range was changed to 0.4 ng/ml.

Conclusions: Measurement of serum TSH in dogs has excellent specificity and is useful in confirming hypothyroidism, but its low sensitivity does not allow it to be used to exclude a diagnosis of hypothyroidism.

🌀 CLINICAL IMPACT:

The findings of this study were similar to others, with the exception that others have found a slightly lower specificity of elevated TSH. The authors propose that this may be due to a difference in the TSH response testing and suggest that they may have diagnosed a milder form of hypothyroidism than other researchers. However, they used intramuscular injection of TSH with sampling performed after six hours, while the peak response to TSH given intramuscularly occurs much later. Although the method of TSH response test-

ing in this study may have detected dogs with mild hypothyroidism, there is no evidence to support this presumption. In addition, a more widely accepted method of interpretation of TSH response tests is based solely on absolute T_4 concentration post-TSH rather than a percentage increase above the basal concentration. Although a reference range for T_4 was not given, the finding that 41% of euthyroid dogs had a serum T_4 concentration below 1.5 $\mu\text{g}/\text{dl}$ shows the limitations of a single basal T_4 concentration for diagnosis of hypothyroidism. Current methods of serum TSH measurement in dogs should not be used as sole laboratory evidence of hypothyroidism.



Tryptic Peptides of Canine Thyroglobulin and Autoimmune Thyroiditis

Lee JY, Uzuka Y, Tanabe S, et al. Tryptic peptides of canine thyroglobulin reactive with sera of patients with canine hypothyroidism caused by autoimmune thyroiditis. *Vet Immunol Immunopathol* 2004;101:271-276.

► INTRODUCTION:

Background: Autoantibodies to thyroglobulin (TgAA) are detected in approximately 50% of hypothyroid dogs and are considered a marker of autoimmune thyroiditis. However, TgAA can be found in both euthyroid and hypothyroid dogs. Their presence in euthyroid animals may indicate the presence of lymphocytic thyroiditis, but similar antibodies have been described in humans with other autoimmune thyroid diseases and thyroid neoplasia.

The ability to differentiate antibodies due to autoimmune thyroiditis from those caused by other diseases might be useful in identifying dogs with a genetic predisposition to autoimmune thyroid disease or perhaps predict dogs that are at risk for developing hypothyroidism.

Objectives: The objective of this study was to determine if sera from hypothyroid dogs with TgAA would show specific patterns of reaction to thyroglobulin subject to trypsin digestion.

✕ SUMMARY:

Methods: Thyroglobulin purified from normal canine thyroid glands was partially digested by incubation with trypsin. After separating the tryptic peptides derived from trypsin digestion of thyroglobulin, sera from 10 dogs with hypothyroidism and positive TgAA and from five euthyroid dogs with negative TgAA were tested for reactivity to individual peptides using Western immunoblotting.

Results: Numerous tryptic peptides ranging from 3.5 to 66.2 kDa were derived from trypsin digestion of canine thyroglobulin. All sera from hypothyroid dogs reacted with peptides with molecular weights of 43, 32.5, and 31 kDa, while none of the sera from normal dogs reacted. Some of the sera from both normal and hypothyroid dogs reacted

with small peptides of less than 14.4 kDa.

Conclusions: Further study of tryptic peptides of thyroglobulin may allow identification of specific antigenic epitopes that could help define the pathogenesis of autoimmune thyroiditis.

Numerous tryptic peptides were derived from trypsin digestion of canine thyroglobulin.



CLINICAL IMPACT:

The significance of a positive TgAA titer in a euthyroid dog is unclear. It could mean that the dog has autoimmune thyroiditis that could lead to hypothyroidism in the future or that the trait for development of thyroiditis may be passed genetically to offspring. Alternatively, other diseases, such as thyroid neoplasia or thyroiditis unrelated to autoimmunity, could be associated with a positive TgAA. It is possible that evaluation of tryptic peptides of thyroglobulin could aid in determining the significance of TgAA. Longitudinal studies of euthyroid dogs with TgAA will be necessary to determine the significance of these autoantibodies in the development of hypothyroidism or propagation of thyroid autoimmunity as a genetic disorder. It is also possible that dogs with thyroid carcinomas could have antibodies against epitopes on thyroglobulin that could be detected using tryptic peptides. This study answered none of these clinically relevant questions, but it does lay the foundation for further studies that may provide the answers.



Transdermal Methimazole for the Treatment of Feline Hyperthyroidism

Sartor LL, Trepanier LA, Kroll MM, et al. Efficacy and safety of transdermal methimazole in the treatment of cats with hyperthyroidism. *J Vet Intern Med* 2004;18:651-655.

► INTRODUCTION:

Background: Transdermal administration of drugs has gained popularity recently in veterinary medicine. This reduces the burden of medication administration associated with chronic oral medications in some patients and could improve compliance. Methimazole in a pluronic lecithin organogel (PLO) is frequently administered to cats with hyperthyroidism. Although a pharmacokinetic study showed inconsistent and poor absorption of transdermal methimazole in PLO gel after a single dose, it appears to be effective based on clinical experience.

Objectives: The primary objectives of this study were to evaluate the efficacy and safety of methimazole administered transdermally to cats with hyperthyroidism.

✦ SUMMARY:

Methods: Forty-seven cats with newly diagnosed hyperthyroidism were randomly assigned to receive methimazole by either transdermal or oral administration at a dosage of 2.5 mg twice daily. The methimazole gel was applied to the inner pinnae, alternating ears with each application. History, physical examination, complete blood count, serum biochemistries, urinalysis, body weight, serum T₄ concentration, and systolic blood pressure were measured prior to and at two and four weeks after initiating treatment.

Results: Of the 47 cats enrolled in the study, 44 participated enough to be included, including 17 cats in the oral group and 27 in the transdermal group. The two groups were similar in all parameters prior to treatment except the transdermal group had a significantly higher serum alanine aminotransferase activity than the oral group. Most measures of clinical response and changes in serum biochemistries and blood pressure

were similar between the groups.

Serum T₄ concentration decreased in both treatment groups after two and four weeks of treatment but decreased significantly more in the oral group than the transdermal group at two weeks. Significantly more cats in the oral group (14 of 16) had serum T₄ in the reference range than the transdermal group (14 of 25). By week 4 of treatment, the difference in T₄ between the treatment groups was similar, but no longer statistically significant to that at week 2, probably because the number of cats evaluated at four weeks was considerably less (11 oral and 21 transdermal).

A higher incidence of adverse effects related to the gastrointestinal tract were noted in the oral group (4/17) compared with the transdermal group (1/27). One cat with vomiting and anorexia on oral methimazole tolerated transdermal administration without adverse effects. No difference in adverse effects of methimazole manifested as neutropenia, facial excoriation, or hepatopathy were noted between treatment groups.

Conclusions: While both routes of administration are efficacious, oral treatment is more effective at a given dose. Adverse effects are fewer with transdermal administration.

🌀 CLINICAL IMPACT:

Based on this study, methimazole is effective when administered as a transdermal gel, although a higher dose may be necessary to have effects equivalent to the drug administered orally. Transdermal administration is generally well tolerated by cats and readily accomplished by owners. Because vomiting and anorexia are common adverse effects in cats administered methimazole orally, transdermal administration might be useful in cats that do not tolerate the drug orally. Transdermal

preparations must be compounded by a pharmacy. Because there may be variation between pharmacies in the specific preparation used and because of the potential for variation from a pharmacy's batch to batch, the clinician must be particularly vigilant in monitoring clinical response and serum T₄ concentrations.

Transdermal administration might be useful in cats that do not tolerate the drug orally.



Serum 25-Hydroxycholecalciferol and 1,25-Dihydroxycholecalciferol in Dogs

Gerber B, Hauser B, Reusch CE. Serum levels of 25-hydroxycholecalciferol and 1,25-dihydroxycholecalciferol in dogs with hypercalcemia. *Vet Res Commun* 2004;28:669-680.

► INTRODUCTION:

Background: Vitamin D is absorbed in the small intestine and hydroxylated in the liver to 25-hydroxycholecalciferol (25-OH-D₃). It circulates in the bloodstream or is stored in the liver. Under certain stimuli 25-OH-D₃ undergoes further hydroxylation in the epithelial cells of the proximal renal tubules by activation of the enzyme, 1 α -hydroxylase, to the most potent form of vitamin D: 1,25-dihydroxycholecalciferol (1,25-(OH)₂-D₃). Increased production of parathyroid hormone (PTH) or decreased serum concentrations of phosphorus, calcium, or 1,25-(OH)₂-D₃ are stimuli for increased production of 1,25-(OH)₂-D₃. Hypercalcemia suppresses production of 1,25-(OH)₂-D₃ directly on the renal tubules and indirectly by inhibiting PTH production. **Objectives:** The goals of this study were to compare the serum concentrations of 25-OH-D₃ and 1,25-(OH)₂-D₃ among dogs with hypercalcemia from various causes. The effects of regulators of 1,25-(OH)₂-D₃ were also compared to assess diagnostic value.

✕ SUMMARY:

Methods: Twenty-four healthy dogs of both sexes and various ages served as controls. Hypercalcemic dogs included 12 with lymphoma, five with primary hyperparathyroidism, and 10 with chronic renal failure. Nearly all dogs had the following routine laboratory evaluations performed: hemogram and serum bilirubin, glucose, urea, creatinine, total protein, albumin, cholesterol, sodium, potassium, chloride, calcium, and phosphorus concentrations. Urinalysis was performed and activities of alkaline phosphatase, alanine transferase, aspartate transferase, and amylase were measured. Serum assays of 25-OH-D₃; 1,25-(OH)₂-D₃;

and PTH were performed at least weekly.

Results: Serum 1,25-(OH)₂-D₃ concentrations in dogs with lymphoma, primary hyperparathyroidism, and chronic renal failure were 26 to 332 pmol/L (median, 110 pmol/L), 61 to 398 pmol/L (median, 248 pmol/L), and 28 to 310 pmol/L (median, 88.5 pmol/L), respectively. Normal reference range from control dogs was 60 to 239 pmol/L, median of 157.5 pmol/L. No significant differences in serum 1,25-(OH)₂-D₃ concentrations were found among dogs with hypercalcemia.

Serum 25-OH-D₃ concentrations in dogs with lymphoma, primary hyperparathyroidism, and chronic renal failure were 64 to 291 nmol/L (median, 101.5 nmol/L), 66 to 298 nmol/L (median, 91 nmol/L), and 35 to 184 nmol/L (median, 67 nmol/L), respectively. Normal reference range was 48 to 350 nmol/L, median of 306.5 nmol/L. Hypercalcemic dogs had significantly lowered serum 25-OH-D₃ concentrations compared to control dogs.

Dogs with primary hyperparathyroidism were significantly older than dogs with lymphoma.

Conclusions: Serum concentrations of 25-OH-D₃ and 1,25-(OH)₂-D₃ are not predictable in dogs with hypercalcemia.

🌀 CLINICAL IMPACT:

Serum concentrations of 25-OH-D₃ are not regulated within a narrow range and do not change rapidly due to the long biological half-life (duration of action is about a month). Dietary intake, intestinal absorption, and hepatic hydroxylation of vitamin D affect 25-OH-D₃ serum concentration. Dogs with lymphoma, primary hyperparathyroidism, or chronic renal failure have variable appetite, intestinal adsorption of fat-soluble vitamins,

and hepatic concentrations of 25-hydroxylase. For these reasons and perhaps more, the diagnostic utility of measuring serum 25-OH-D₃ concentrations to differentiate the causes of hypercalcemia is poor.

In turn, 25-OH-D₃ is the precursor for 1,25-(OH)₂-D₃. The production rate of 1,25-(OH)₂-D₃ is affected in part by the quantity of circulating 25-OH-D₃. In addition, the quantity and activity of 1 α -hydroxylase is affected by chronic renal disease and hypercalcemic nephropathy. Serum concentrations of 25-OH-D₃ and 1,25-(OH)₂-D₃ are not of value in differentiating three diseases in this study that can cause hypercalcemia. Determination of serum levels of 25-OH-D₃ and 1,25-(OH)₂-D₃ are warranted if the cause of hypercalcemia has not been determined and hypervitaminosis D has not been ruled out.

Serum concentrations of 25-OH-D₃ and 1,25-(OH)₂-D₃ are not of value in differentiating three diseases in this study.



Plasma-Ionized Magnesium Concentration in Dogs with Diabetes Mellitus

Fincham SC, Drobatz KJ, Gillespie TN, et al. Evaluation of plasma-ionized magnesium concentration in 122 dogs with diabetes mellitus: a retrospective study. *J Vet Intern Med* 2004;18:612-617.

► INTRODUCTION:

Background: Plasma magnesium concentrations are frequently decreased in humans and cats with diabetes mellitus. This occurs secondary to urinary loss due to polyuria and because of acidosis. Hypomagnesemia can cause insulin resistance and may contribute to hypertension, cardiac arrhythmias, and neuromuscular weakness. Because serum total magnesium concentration is affected by acid-base balance, hydration status, insulin activity, and plasma proteins, ionized magnesium concentrations are necessary to most accurately assess magnesium status.

Objectives: The objective of this study was to determine if abnormalities in magnesium occur in dogs with diabetes mellitus.

✕ SUMMARY:

Methods: Case records of dogs with diabetes mellitus that had ionized magnesium concentration evaluated were reviewed. Dogs were classified as having uncomplicated diabetes mellitus, diabetic ketoacidosis, or ketotic nonacidotic diabetes mellitus (ketonuria without acidosis). They were also categorized as either receiving insulin treatment prior to evaluation or not. Dogs that had been previously treated with insulin were classified as poorly controlled or not poorly controlled. Normal plasma ionized magnesium was established using the two standard deviations above and below the mean of 22 normal dogs. In addition, ionized magnesium in 19 dogs with acute pancreatitis was evaluated because many of the dogs with diabetic ketoacidosis had concurrent acute pancreatitis.

Results: Records of 122 diabetic dogs were reviewed. Uncomplicated diabetes mellitus was present in 78, ketoacidosis in 32, and ketonuria without acidosis in 12. Concurrent

disease was present in 71% of all dogs, with acute pancreatitis (15%), hyperadrenocorticism (11%), urinary tract infection (11%), and neoplasia (7%) being the most common disorders. Acute pancreatitis was diagnosed in 47% of dogs with ketoacidosis. Plasma ionized magnesium concentration was significantly higher in dogs with ketoacidosis than those with uncomplicated diabetes mellitus or normal dogs. Ionized magnesium

Measurement of plasma ionized magnesium should be considered in those with insulin resistance, persistent hypertension, weakness, or cardiac arrhythmias.

was not different in dogs with diabetes mellitus or pancreatitis without diabetes compared with normal dogs. Dogs with uncomplicated diabetes, ketonuria without acidosis, or ketoacidosis had plasma ionized magnesium below the reference range in 23%, 17%, and 6% of cases. Ionized magnesium was above the reference range in 48% of dogs with ketoacidosis, 25% of dogs with ketonuria without acidosis, and 18% of dogs with uncomplicated diabetes. The pH and bicarbonate content of venous blood was inversely correlated with the ionized magnesium concentration. Prior insulin administration was not associated with changes in plasma ionized magnesium concentrations. There was no significant difference between ionized magnesium in dogs with poorly controlled diabetes and those that were not poorly controlled.

Conclusions: Most dogs with diabetes mellitus do not have hypomagnesemia.

🌀 CLINICAL IMPACT:

The finding that hypomagnesemia was uncommon in dogs with diabetes mellitus is significant because ionized magnesium is infrequently measured in veterinary practice. Because total magnesium correlates poorly with ionized magnesium in cats with diabetes mellitus, it is important to use caution when assessing

the importance of any decrease in plasma total magnesium concentration. Despite the infrequent occurrence of hypomagnesemia in diabetic dogs, measurement of plasma ionized magnesium should be considered in those with insulin resistance, persistent hypertension, weakness, or cardiac arrhythmias.



Hyperglycemic, Hyperosmolar Syndrome in Feline Diabetics

Koenig A, Drobatz KJ, Beale AB, et al. Hyperglycemic, hyperosmolar syndrome in feline diabetics: 17 cases (1995-2001). *J Vet Emerg Crit Care* 2004;14:30-40.

► INTRODUCTION:

Background: Hyperglycemic hyperosmolar syndrome (HHS), previously called hyperglycemic hyperosmolar nonketotic diabetic coma, is a rare complication of diabetes mellitus. It is characterized by markedly elevated blood glucose and dehydration leading to hyperosmolality, without ketone body formation. Concurrent disease, impaired renal function, and abnormal mentation occur commonly in patients with HHS. Mortality is high with this syndrome.

Objectives: The objectives of this retrospective study were to characterize the clinical findings of HHS in cats and to determine the outcome and prognostic indicators for survival.

✦ SUMMARY:

Methods: Medical records from all diabetic cats admitted over a six year period were reviewed and included in the study if they had blood tests performed at the time of admission to an emergency service and were not presented because of a hypoglycemic crisis. Cats with a serum glucose concentration at least 600 mg/dl and a calculated total serum osmolality at least 350 mOsm/kg and negative urine ketones were classified as HHS. Cats with measurable ketones in the urine were assigned to the diabetic ketoacidosis group, while cats with diabetes but negative ketones and total calculated osmolality less than 350 mOsm/kg were assigned to the diabetes mellitus group. Information relating to signalment, history, previous treatment, physical examination, laboratory test results, length of hospitalization, and survival were compared among the three groups of diabetic cats.

Results: Hyperglycemic hyperosmolar syndrome was found in 17 of 134 diabetic cats. Diabetic ketoacidosis was found in 37 and uncomplicated diabetes mellitus in

80 cats. Twelve of the cats with HHS were previously diagnosed with diabetes mellitus and were receiving insulin treatment for a median of 18 months prior to diagnosis of HHS. Two cats with HHS had previously been diagnosed with diabetic ketoacidosis. The duration of diabetes, dose of insulin, insulin type, and duration of illness prior to presentation were not different between the three groups of diabetic cats.

Clinical signs of cats with HHS (from most to least frequent) included polyuria and polydipsia, anorexia, lethargy, vomiting, ataxia or weakness, respiratory problems, weight loss, inappropriate elimination, and neurologic signs including circling, pacing, and unresponsiveness. Abnormalities on physical examination included dehydration in 14, hypothermia in nine, heart murmur in four, cardiac arrhythmia in one, renomegaly in two, and a variety of other abnormalities related to concurrent disorders. Neurologic abnormalities included depression in 11 and stupor in two, while nine cats had other neurologic deficits including plantigrade stance, profound weakness, abnormal pupillary light reflexes, absent menace reflex, absence of all cranial nerve reflexes, and seizures.

Anemia was present in three cats with HHS, a moderate number of Heinz bodies were apparent in four, and a mature neutrophilia was present in eight. The mean blood glucose concentration in cats with HHS was 748 mg/dl, while it was 350 mg/dl and 366 mg/dl for the ketoacidosis and uncomplicated diabetes mellitus groups, respectively. The mean calculated total serum osmolality was 384 mOsm/kg for HHS cats, 354 mOsm/kg for cats with diabetic ketoacidosis, and 351 mOsm/kg for cats with uncomplicated diabetes. Azotemia was present in nearly all cats with HHS. In

addition, elevated AST, hyperphosphatemia, acidosis, hypochloremia, and elevated lactate were common. Among 17 cats, chronic renal failure was present in 10, concurrent infection in eight, congestive heart failure in five, and neoplasia in four were significantly more common in cats with HHS than in cats in one or both of the other groups. Only six of the 17 (35%) cats with HHS survived hospitalization, and the survival rate was significantly lower than for cats with ketoacidosis (84%) or uncomplicated diabetes (81%).

Conclusions: Hyperglycemic hyperosmolar state is commonly associated with concurrent disease and mortality is very high.

CLINICAL IMPACT:

This is the first description of a series of cases of hyperglycemic hyperosmolar state in cats. This disorder accounted for less than 10% of emergency presentations for cats with diabetes mellitus, and thus is uncommon.

It is important to recognize that severe hyperglycemia, marked hyperosmolality in the absence of ketones is associated with a poor prognosis in cats. A thorough search for concurrent disease is essential in these cases and may influence prognosis to a greater degree than the HHS. Blood glucose concentration does not exceed 500 mg/dl if glomerular filtration is adequate. HHS is caused by poor renal perfusion or renal disease. Not surprisingly, renal failure was the most common concurrent problem in most of the cats in this study with HHS.

Renal failure was the most common concurrent problem in most of the cats in this study with HHS.



Funduscopy Findings Following Phacoemulsification in Diabetic Dogs

Landry MP, Herring IP, Panciera DL. Funduscopy findings following cataract extraction by means of phacoemulsification in diabetic dogs: 52 cases (1993-2003). *J Am Vet Med Assoc* 2004;225:709-716.

► INTRODUCTION:

Background: Diabetic retinopathy is a leading cause for blindness in humans, but it is believed to be rare and subclinical in diabetic dogs. Vision-impairing diabetic retinopathy in humans requires months or years to develop. Cataracts are more common in dogs and have a rapid onset of a few weeks if glycemic control is poor or nonexistent. Funduscopy examination in clinical cases of dogs may not have been reassessed long enough after cataract removal to detect the true incidence of diabetic retinopathy in the dog.

Objectives: The purpose of the study was to determine the presence of microaneurysms and retinal hemorrhages in diabetic dogs after phacoemulsification and to identify risk factors.

✕ SUMMARY:

Methods: The medical records of 52 diabetic dogs and 174 dogs that underwent phacoemulsification were reviewed for signalment, history, physical exam findings, ophthalmologic exam findings, laboratory findings, electroretinographic findings, and surgical findings. The administration of nonsteroidal anti-inflammatory drugs was recorded because of their potential to prolong bleeding times. Blood glucose control was categorized as poor, intermediate, or good based on blood glucose concentration, changes in body weight, required insulin dosage, and the presence of glucosuria or ketonuria.

Results: Twenty-one percent (11 of 52) of diabetic dogs had retinal hemorrhages or microaneurysms. Only 0.6% (1 of 174) of nondiabetic dogs had either retinal lesion. The median time from onset of diabetes mellitus to the diagnosis of retinal lesions was 1.4 years (0.5 to 3.2 years). There were no identified

predisposing factors for retinopathy.

Conclusions: Retinal hemorrhages and microaneurysms are more common and develop earlier in diabetic dogs than previously believed.

🌀 CLINICAL IMPACT:

There are two forms of diabetic retinopathy in humans. Background retinopathy is the most common form in insulin-independent diabetic humans, eventually affecting about 15%. Proliferative retinopathy is more common in insulin-dependent diabetics typically appearing seven to 10 years after the initial diagnosis of diabetes. Approximately 25% of insulin-dependent diabetics have proliferative retinopathy after 15 years from initial diagnosis. Proliferative retinopathy can progress to vitreal hemorrhage or retinal detachment, the ultimate causes of diabetic blindness in humans.

Since dogs typically have insulin-dependent diabetes mellitus, proliferative retinopathy and blindness would seem to be a risk if dogs survived after diagnosis of diabetes an equivalent to diabetic humans' seven to 15 years. However, this has not been the observation clinically. The results of this study substantiate the clinical observations: background retinopathy can develop in about 20% of diabetic dogs undergoing phacoemulsification in less than a year from the onset of diabetes with a median of approximately 1.5 years, but vitreal hemorrhage, retinal detachment, and subsequent blindness from retinopathy do not occur.

There were no identified predisposing factors for retinopathy.



Canine Gastrinoma

Fukushima R, Ichikawa K, Hirabayashi M, et al. A case of canine gastrinoma. J Vet Med Sci 2004;66:993-995.

► INTRODUCTION:

Background: Many tumors of the pancreatic islets are possible, but insulinomas are the most common followed distantly by gastrinomas. Gastrinomas are pancreatic islet cell tumors that secrete excessive gastrin which causes gastric hyperacidity and eventually gastric and duodenal ulceration. Few gastrinomas have been reported in dogs, but the signs produced by gastrinomas, vomiting and diarrhea, have a multitude of possible causes. The low index of suspicion for gastrinomas as a cause of vomiting and diarrhea in dogs probably contributes to the paucity of reports.

Objectives: The reason for this report was to describe the clinical signs and ultrasonographic, endoscopic, laboratory, and necropsy findings in a dog with a gastrinoma.

✦ SUMMARY:

Case Report: A 10-year-old, castrated male, Shih Tzu was presented with a history of persistent vomiting and anorexia for a month. Physical findings were emaciation and rough hair coat. Laboratory findings were a mild leukocytosis and left shift plus a marked hypoproteinemia (4.2 g/dl) and hypokalemia (2.7 mEq/L). Routine abdominal radiography findings were within normal limits. Abdominal ultrasonography revealed an irregular contour of the gastric mucosa and unusual pattern around the lower pyloric portion of the greater curvature of the stomach. Gastroscopy demonstrated a gastric ulcer, pyloric stenosis, and petechial hemorrhages. Based on these findings chronic gastritis was diagnosed, and treatment was begun with H₂ blockers and metoclopramide. Clinical signs improved gradually over several days.

Three months later, the dog was

presented again for vomiting. Treatment with metoclopramide and amoxicillin for *Helicobacter* led to temporary improvement.

Fasting serum gastrin was measured and found to be 5 to 10 times the upper limit of normal (410 pg/ml). Surgery was not possible, and symptomatic therapy had variable responses. The dog died four months later.

Just prior to the dog's death a hemogram revealed normocytic anemia (packed cell volume of 32.7%) and leukocytosis (31,800/ μ l). The earlier hypoproteinemia persisted (4.4 g/dl), but the serum potassium

had increased to hyperkalemic range (5.7 mEq/L). Necropsy revealed intestinal fluid in the peritoneal cavity and perforated duodenal ulcers. Clusters of tumor cells were found in the pancreas. The majority of tumor cells stained positive for gastrin. The tumor was diagnosed as a gastrinoma.

Conclusions: Dogs with refractory gastritis should be evaluated for possible gastrinoma.

🌀 CLINICAL IMPACT:

Dogs with a history of vomiting refractory to eliminating dietary indiscretions and medications or that vomit blood without evidence of a gastric foreign body or hemostasis problem should be evaluated for gastrinoma. Fasting gastrin concentrations are the only presurgical diagnostic method with any reliability. Because antisecretory drugs can markedly increase gastrin secretion, testing should be performed in the absence of H₂ blockers or proton pump inhibitors. Abdominal imaging is often inconclusive with gastrinomas although pyloric hypertrophy is often present. The only effective treatment for gastrinoma is early detection and excision.

The dog in this report was not described as

having diarrhea, but diarrhea can be a clinical sign directly related to gastric hyperacidity and maldigestion from gastrinoma. A dog with gastric or duodenal ulcers and diarrhea should be evaluated for gastrinoma.

Multiple types of tumors were not reported in this case. Humans with multiple gastrinoma tumors may have Multiple Endocrine Neoplasia 1. MEN 1 is an inherited tardive endocrinopathy. Nearly all cases in humans also have hyperparathyroidism. The report of this dog does not rule-out MEN-1. Serum calcium and phosphorus concentrations or the post-mortem appearance of the parathyroid glands were not mentioned.

Dogs with refractory gastritis should be evaluated for possible gastrinoma.



Adrenal Steroid Hormone Concentrations in Dogs with Alopecia X

Frank LA, Hnilica KA, Oliver JW. Adrenal steroid hormone concentrations in dogs with hair cycle arrest (alopecia X) before and during treatment with melatonin and mitotane. *Vet Dermatol* 2004;15:278-284.

INTRODUCTION:

Background: Alopecia X is a disorder characterized by partial to complete alopecia involving the neck, trunk, caudal thighs, and perineum that occurs in young adult to middle-aged dogs. Dogs are otherwise free of clinical signs, have normal thyroid function and cortisol responses to adrenocorticotropic hormone (ACTH) and dexamethasone administration. It is not clear if excessive secretion of adrenal steroid hormones are involved in the pathogenesis of the hair loss.

Objectives: The objectives of the study were to determine if melatonin is an effective treatment for Alopecia X and to determine if hair regrowth is associated with changes in adrenal steroid hormone concentrations.

SUMMARY:

Methods: Alopecia X was diagnosed in 29 neutered dogs (15 male, 14 female) based on clinical signs, normal thyroid function testing, and normal cortisol concentration after ACTH administration or low-dose dexamethasone suppression testing. The dogs were evaluated during the study by an unspecified number of veterinarians and all hormone assays were performed at the authors' laboratory. Serum concentrations of progesterone, 17-hydroxyprogesterone, androstenedione, testosterone, estradiol, and cortisol were measured before and after administration of cosyntropin at the time of the initial evaluation and every four months for up to one year.

Dogs were administered melatonin orally (3 mg twice daily if less than 15 kg and 6 mg twice daily if more than 15 kg). At each four month recheck, the percentage of body affected by alopecia and the quality of the hair coat was assessed in addition to performing the ACTH response test. If the hair regrowth

was inadequate and based on owner's wishes, the dose of melatonin was increased.

Results: Twenty-five of the dogs were evaluated at least twice, while 23 dogs were evaluated for an entire year. Pomeranians comprised the majority of cases (23 dogs), while keeshond, miniature poodle, and Siberian husky were the other breeds studied. Hair regrowth was complete (defined as "less than 25% of the body affected and moderate undercoat with partial to complete guard hair re-growth") in four dogs, while partial regrowth occurred in 14 dogs for an overall response to melatonin of 62%.

The dose of melatonin was increased in eight dogs with either no or partial hair regrowth. Only one dog (with partial hair regrowth on the lower dose) had a response to the higher melatonin dose. Two dogs developed occasional lethargy and one had increased flatulence during melatonin treatment. Prior to treatment, basal serum concentrations of progesterone, androstenedione, and 17-hydroxyprogesterone in Pomeranians were above the reference range in 68%, 65%, and 35%, respectively, while the post-ACTH concentrations of these hormones were elevated in 84%, 26%, and 25%, respectively. There was no difference in baseline or post-ACTH steroid hormone concentrations after four months of melatonin treatment, with the exception of an increase in post-ACTH 17-hydroxyprogesterone.

Mitotane was administered to six dogs after no response (five dogs) or partial response (one dog) to melatonin treatment. Hair regrowth was complete in three and partial in two dogs during mitotane treatment. Suppression of serum cortisol concentrations occurred in only two of the dogs treated with mitotane, and both these dogs still had

baseline serum concentrations of progesterone, 17-hydroxyprogesterone, and androstenedione that were above the reference range.

Conclusions: Hair regrowth in dogs with Alopecia X is not mediated by changes in adrenal steroid hormones.



CLINICAL IMPACT:

Despite the finding that many dogs with Alopecia X have elevated adrenal steroid hormone concentrations, it does not appear that resolution of these abnormalities are necessary for hair regrowth. Because of the preponderance of Pomeranian dogs in this study, it is possible that this breed normally has higher serum steroid hormone concentrations than other breeds, which could account for the elevations noted. The efficacy of melatonin treatment is not clear because it is not known how many dogs in this study would have had hair regrowth without any treatment.

Hair regrowth in dogs with Alopecia X is not mediated by changes in adrenal steroid hormones.



Otic Glucocorticoids and Adrenal Function

Ghubash R, Marsella R, Kunkle G. Evaluation of adrenal function in small-breed dogs receiving otic glucocorticoids. *Vet Dermatol* 2004;15:363-368.

► INTRODUCTION:

Background: Topical administration of glucocorticoids invariably results in some systemic absorption. The absorbed exogenous glucocorticoid has an additive effect to endogenous glucocorticoids on the negative glucocorticoid feedback to the hypothalamus and pituitary. Usually the amount is inconsequential to organ function with the exception of the feedback on adrenocorticotrophic hormone (ACTH) secretion. If the administration is more frequent than the time for recovery of ACTH secretion, persistent lack of ACTH stimulation on the adrenal cortex for a week or more will result in adrenocortical atrophy. Accurate estimates for the time required for recovery from hypothalamic-pituitary adrenal axis suppression from frequent otic glucocorticoid treatment are not known.

Objectives: The purpose of this study was to assess the adrenocortical function of small dogs treated with otic preparations containing dexamethasone or betamethasone and the recovery from suppression after otic glucocorticoid treatment withdrawal.

✕ SUMMARY:

Methods: Fourteen healthy small breed dogs were administered an otic preparation containing either dexamethasone (Tresaderm®, Merial Limited, Iselin, NJ) or betamethasone (Otomax®, Schering-Plough Animal Health Corp., Union, NJ) at manufacturer's recommended dosage (10 drops and four drops, respectively) twice per day in both ear canals for two weeks. Adrenocortical function was assessed by ACTH stimulation testing before and immediately after ceasing the two week long treatment. Follow-up ACTH stimulation testing was continued weekly until recovery of adrenocortical function was evident.

Results: All dogs that received the otic

preparation with betamethasone and two dogs that received dexamethasone otic preparation had adrenocortical function within normal limits after two weeks of treatment. Five of the seven dogs (73.4%) receiving otic dexamethasone treatment had suppressed adrenocortical function after the two week long treatment. Three of the five dogs with suppressed adrenocortical function returned to normal within a week of discontinuing the otic administrations. The other two of the five adrenocortical suppressed dogs regained normal function within the second week after discontinuing otic administrations.

Conclusions: Adrenocortical function can be suppressed for up to two weeks in dogs receiving otic dexamethasone.

🌀 CLINICAL IMPACT:

Betamethasone and dexamethasone are nearly equipotent glucocorticoids. Betamethasone is slightly more potent per mg. However, in this study, otic dexamethasone caused more systemic absorption effects. The reasons are probably that twice the volume and twice the dose in mg of dexamethasone was used in comparison to otic betamethasone.

How the results of this study relates to clinical situations is unknown. The dogs in this study had normal external ear canals, but these preparations are for use in dogs that have inflamed ear canals. Inflamed otic epithelium would permit greater systemic absorption of otic glucocorticoids than non-inflamed epithelium would. Therefore, the risks of adrenocortical suppression from otic glucocorticoid treatment may be greater than indicated in this report. Conversely, the manufacturers' recommendation for either of the preparations in the present study are for only one week of treatment. Dogs were treated for two weeks in this study. Dogs treated

according to manufacturers' recommendation may not develop suppressed adrenocortical function.

If equal dosage in mg and volume of otic preparations are administered, the same degree of adrenocortical suppression should be expected from dexamethasone and betamethasone otic preparations.

The same degree of adrenocortical suppression should be expected from dexamethasone and betamethasone otic preparations.



Plasma Renin Activity, Adrenocortical Hormones, and α -Melanocyte-Stimulating Hormone in Cats

Javadi S, Slingerland LI, van de Beck MG, et al. Plasma renin activity and plasma concentrations of aldosterone, cortisol, adrenocorticotropic hormone, and α -melanocyte-stimulating hormone in healthy cats. *J Vet Intern Med* 2004;18:625-631.

► INTRODUCTION:

Background: Cats with systemic hypertension with and without renal disease, aldosteronomas, or hypokalemic myopathy are receiving greater recognition and attention in recent years. However, the role of the endocrine system in the pathogenesis of cardiovascular diseases such as systemic arterial hypertension or hypokalemic myopathy is not well understood primarily because the normal reference ranges for renin activity and aldosterone in older pet cats have not been established on a large group of healthy house cats. Knowledge of the endocrine system roles in causing or mediating cardiovascular disease could lead to selection of more effective medications for management.

Objectives: The goals of this study were to establish normal reference ranges for plasma renin activity and concentrations of aldosterone in cats. Possible normal variables that alter plasma cortisol, adrenocorticotropic hormone (ACTH), and α -melanocyte-stimulating hormone (α -MSH) concentrations were also assessed.

✕ SUMMARY:

Methods: One hundred and thirty healthy house cats of various breeds with normal plasma urea and creatinine concentrations were subjects for establishing normal reference ranges for plasma renin activity and aldosterone concentration in cats. Plasma cortisol, ACTH, α -MSH, and glucose concentrations and creatine kinase activity were also measured.

Results: Plasma renin activity ranged from 60 to 630 fmol/L/s (0.3 to 3 ng/ml/h). Plasma aldosterone concentrations ranged from 110 to 540 pmol/L (40 to 195 pg/ml). The aldosterone-to-renin ratio was 0.3 to 3.8.

There were no significant breed differences in reference ranges. Aldosterone-to-renin ratios were significantly higher in cats 5-years of age, or more, compared to younger cats and in neutered cats compared to intact cats. The change in aldosterone-to-renin ratios were caused by lower renin activity in older cats and neutered cats. Plasma concentrations of ACTH, α -MSH, and cortisol were not correlated with aldosterone-to-renin ratio.

Conclusions: Normal reference ranges for plasma renin activity and concentrations of aldosterone in house cats are similar to normal human reference ranges.



CLINICAL IMPACT:

Normal reference ranges for aldosterone and renin in house cats will be useful reference for evaluating cats with systemic hypertension, hypokalemia, or adrenal enlargement. Causes for lower plasma renin activity in neutered cats and aged cats are unclear.

The change in aldosterone-to-renin ratios were caused by lower renin activity in older cats and neutered cats.



Urinary Corticoid: Creatinine Ratios After Oral Low-Dose Dexamethasone Suppression

Vaessen MMAR, Kooistra HS, Mol JA, et al. Urinary corticoid:creatinine ratios in healthy pet dogs after oral low-dose dexamethasone suppression tests. *Vet Rec* 2004;155:518-521.

► INTRODUCTION:

Background: Hyperadrenocorticism either involves an insensitivity to glucocorticoid feedback on adrenocorticotropic hormone (ACTH) production or autonomous secretion of cortisol from an adrenal tumor. In both cases, low-dose dexamethasone administration does not cause a decrease in ACTH secretion or, in turn, a decrease in plasma cortisol secretion. Low-dose dexamethasone suppression testing has poor specificity but good sensitivity in the diagnosis of hyperadrenocorticism in dogs. As a result, low-dose dexamethasone suppression is a good screening test for hyperadrenocorticism.

In the United States, low-dose dexamethasone testing is usually performed by obtaining plasma samples before the intravenous administration of dexamethasone and at multiple different times after dexamethasone administration. Urine corticoid is a product of glomerular clearance of free cortisol. Urine corticoid concentration corrected for urine concentration by comparison with urine creatinine is indicative of adrenocortical activity over several hours rather than minutes as reflected by plasma concentration of cortisol. The optimum dose of oral dexamethasone for a low-dose dexamethasone test using urine corticoid-to-creatinine ratio to monitor suppressibility is not known.

Objectives: To establish a suitable dose of dexamethasone for low-dose dexamethasone testing in dogs using urinary corticoid-to-creatinine ratio as the means to monitor response.

✦ SUMMARY:

Methods: Owners of 11 healthy pet dogs collected urine samples from their dogs at

two hour intervals from 8 a.m. to 10 p.m. for control values of urinary corticoid-to-creatinine ratio. The same procedure was performed in seven dogs on three additional days with a week between each period of urine collection. Dexamethasone was

A single oral dose of 0.01 mg/kg of dexamethasone to healthy dogs causes a reduction of urinary corticoid-to-creatinine ratio by at least 50%.

administered orally at each collection day immediately after the 8 a.m. urine collection. The dexamethasone doses of 0.02 mg/kg, 0.01 mg/kg, and 0.0075 mg/kg were evaluated in each dog.

Results: All doses of dexamethasone caused a decline in urine corticoid-to-creatinine ratios with a minimum at eight hours after dexamethasone administration. The reduction was more than 50% of the early morning values following the doses of 0.02 and 0.01 mg/kg of dexamethasone. The dose of 0.0075 mg/kg did not cause a reduction of 50% and the reduction was not significant.

Conclusions: A single oral dose of 0.01 mg/kg of dexamethasone to healthy dogs causes a reduction of urinary corticoid-to-creatinine ratio by at least 50%. This provides a less stressful, at home, means of collecting clinical samples for screening for excessive adrenocortical function.

🌀 CLINICAL IMPACT:

The oral administration of dexamethasone for adrenocortical suppression testing in dogs has been previously described as a multiple dose method before urine samples are collected for corticoid-to-creatinine ratio determination. The results of this study indicate a single oral 0.01 mg/kg dose of dexamethasone is effective in suppressing the adrenal cortex for testing for normalcy and is as effective as intravenous dexamethasone. The oral method can be less stressful to the patient and less expensive due to the lack of hospitalization and serum collection. However,

many clients may not be persuaded to collect urine from their dog, or may not be able to reliably administer the oral dexamethasone. The results of this study are not applicable to cats because cats are more resistant to dexamethasone suppression than are dogs.



Treatment of Canine Alopecia X with Trilostane

Cerundolo R, Lloyd DH, Persechino A, et al. Treatment of canine alopecia X with trilostane. *Vet Dermatol* 2004;15:285-293.

► INTRODUCTION:

Background: Alopecia X is a poorly understood disorder that is characterized by alopecia and sometimes, hyperpigmentation as the only abnormalities. It occurs predominantly in relatively young, purebred dogs with breed predispositions in Nordic breeds and miniature poodles. While an adrenal enzyme deficiency resulting in elevated plasma 17-hydroxyprogesterone has been implicated in the pathogenesis of this disorder, the true etiology remains unknown.

Objectives: The objective of this study was to evaluate the clinical and endocrinologic responses to trilostane administration in Pomeranian dogs and miniature poodles with Alopecia X.

✕ SUMMARY:

Methods: Alopecia X was diagnosed in 16 Pomeranians (seven spayed females, one intact female, and eight males) and eight miniature poodles (one spayed female, one intact female, and six males) based on the presence of truncal alopecia or "wooly" coat quality, absence of systemic clinical signs, normal results of routine hematology, serum biochemistries, and thyroid function tests; elevation of 17-hydroxyprogesterone before or after adrenocorticotropic hormone (ACTH) administration, or both; and elevated urine cortisol:creatinine ratio. Skin biopsies showed changes consistent with Alopecia X.

All dogs were treated with trilostane orally once per day at the following dosages: less than 2.5 kg - 20 mg; 2.5 to 5 kg - 30 mg; and 5 to 10 kg - 60 mg. Most dogs were rechecked 10 days and four and 12 weeks after initiating trilostane treatment. Evaluation at these times included clinical evaluation, routine hematology, serum biochemistries, urinalysis, and measurement of serum cortisol

and 17-hydroxyprogesterone during an ACTH response test. If no response to treatment was noted after two months, the trilostane dose was doubled. Clinical response was reviewed approximately every six months thereafter.

Results: Hair regrowth was complete in 14 of the 16 dogs, usually beginning within four to eight weeks of instituting treatment. Two Pomeranians required four and six months for hair regrowth that was apparent only after the trilostane dose was doubled. Two other Pomeranians had no hair regrowth after six months of treatment with a trilostane dose of 8.6 and 13.3 mg/kg daily, respectively. The mean dose rate that resulted in hair regrowth was 11.8 mg/kg in Pomeranians and 9 mg/kg in poodles, although doses ranged from 6 to 23.5 mg/kg daily.

After complete hair regrowth, the dosage of trilostane was reduced to an administration on two to three days per week in six dogs without recurrence of alopecia. One dog had thinning of the hair coat after a dose reduction to 20 mg every other day, but it regrew after increasing the dose to 30 mg daily until the coat returned to normal. The dog was then maintained successfully on 30 mg three times per week. In the only two dogs that had treatment stopped after complete hair regrowth, the hair coat remained normal for the seven months of follow-up.

Trilostane treatment suppressed the basal and post-ACTH serum cortisol concentrations, but the serum 17-hydroxyprogesterone concentrations were significantly higher during treatment compared with pretreatment values. Two dogs died during treatment of unknown causes after six and 12 months, respectively.

Conclusions: Trilostane is a safe and effective treatment for Alopecia X.

Trilostane administration was associated with resolution of the alopecia in over 90% of the cases in this study.

🌀 CLINICAL IMPACT:

The pathogenesis of Alopecia X is unknown, and it has not been proven to be related to abnormal adrenal gland function. Unfortunately, details of the hormonal characteristics that led to the diagnosis of Alopecia X in of the dogs in this study were not provided, and the diagnostic criteria for the disease are uncertain.

Regardless, trilostane administration was associated with resolution of the alopecia in over 90% of the cases in this study, and it may have played a therapeutic role. However, seasonal alopecias similar to Alopecia X can occur, and spontaneous recovery among some cases cannot be ruled out. The unexplained death in two dogs of this study during trilostane administration is troublesome and could be related to adrenal insufficiency or adrenal necrosis.



Indicators of Canine Adrenocortical Tumor Malignancy

Labelle P, Kyles AE, Farver TB, et al. Indicators of malignancy of canine adrenocortical tumors: histopathology and proliferation index. *Vet Pathol* 2004;41:490-497.

► INTRODUCTION:

Background: About 15% of dogs with hyperadrenocorticism have adrenal tumors. Based on histopathologic appearance, it is difficult to differentiate some malignant and benign adrenocortical tumors. There is no way to determine the behavior of an adrenocortical tumor on endocrine testing, so gross appearance and histopathology is necessary to determine the tumor type. It is also difficult in some cases to determine if an adrenal tumor is of cortical or medullary origin. Immunohistochemistry can be used to identify characteristics of adrenocortical tumors and may be of use in identifying malignancy.

Objectives: The objectives of this study were to identify histopathologic criteria and an index of cell proliferation to differentiate benign from malignant adrenocortical tumors.

✦ SUMMARY:

Methods: Normal and neoplastic adrenal glands retrieved from pathology archives were evaluated for histopathologic characteristics of malignancy, including size, growth pattern, peripheral fibrosis, capsular or vascular invasion, necrosis, and other findings. In addition, an estimate of cell proliferation was studied by staining tissue using antibody against Ki-67 antigen, a protein expressed in cells that are not in the rest phase (G₀) of the cell cycle. For the purposes of dividing adrenal tumors into groups for study, the tumors were classified as carcinomas if there was histologically confirmed metastasis or vascular invasion. Tumors were classified as adenomas in the absence of metastasis or vascular invasion and if there was disruption of the normal adrenal architecture, compression of the adjacent parenchyma, and the presence of a fibrous capsule surrounding at least part of the tumor. Normal adrenal glands

were studied using the same techniques.

Results: Twenty-six of the tumors were classified as carcinomas. Vascular invasion alone was present in 12, and metastasis was present in 14, 12 of which had vascular invasion as well. Metastasis was found in the liver, lungs, kidneys, ovary, and mesenteric lymph node in nine, seven, two, one, and one cases, respectively.

Adenoma was diagnosed in 23 cases. Carcinomas were significantly larger than adenomas, with all adenomas being smaller than 2 cm while 17 carcinomas were larger than 2 cm. Invasion of the surrounding fibrous capsule was present in 24 carcinomas and in none of the adenomas. Other histopathologic characteristics significantly more common in carcinomas included areas of necrosis or hemorrhage, single cell necrosis, and peripheral fibrosis. Cytoplasmic vacuolation, fibrin thrombi in dilated vessels, and clusters of hematopoietic cells were significantly more common in the adenomas. The proliferation index determined by immunoreactivity for Ki-67 antigen was found to be much higher in carcinomas (mean of 9.3%) than adenomas (0.76%) and normal adrenal glands (0.58%). None of the histologic criteria studied were present in normal adrenal glands.

Conclusions: Histologic criteria and an immunohistochemical estimate of cell proliferation are useful in differentiating malignant and benign adrenocortical tumors in dogs.

🌀 CLINICAL IMPACT:

The importance of determining the malignant nature of a neoplasm lies in determining the prognosis and in making appropriate treatment recommendations. A histologic diagnosis of malignancy carries little meaning if the neoplasm has been completely excised prior

to metastasis. While the findings of this study will help pathologists determine if a tumor is malignant or benign, the clinician will have to use all the clinical data to determine if metastasis or inoperable tumor invasion is present. More extensive knowledge about the metastatic potential of adrenocortical carcinomas and the efficacy of treatments such as chemotherapy for metastatic or inoperable disease is needed.

An immunohistochemical estimate of cell proliferation is useful in differentiating malignant and benign adrenocortical tumors.



Effect of Trilostane on Serum Aldosterone, Cortisol, and Potassium Concentrations in Dogs with Hyperadrenocorticism

Wenger M, Sieber-Ruckstuhl NS, Muller C, et al. Effect of trilostane on serum concentrations of aldosterone, cortisol, and potassium in dogs with pituitary-dependent hyperadrenocorticism. *Am J Vet Res* 2004;65:1245-1250.

► INTRODUCTION:

Background: Mitotane, an adrenocortical cytolytic drug, has been the mainstay of treatment for pituitary-dependent hyperadrenocorticism (PDH) in dogs for 30 years. Trilostane is an alternative medication which inhibits the steroidogenesis enzyme, 3β -hydroxysteroid dehydrogenase, which is required for the synthesis of cortisol and aldosterone and some of their precursors. Although trilostane is usually prescribed to reduce serum cortisol, suppression of aldosterone synthesis is unavoidable. The degree to which aldosterone concentrations are affected by trilostane relative to serum cortisol concentrations is not known in the dog.

Objectives: The purpose of this study was to determine the effect of trilostane on serum concentrations of aldosterone, cortisol, and potassium in dogs with PDH. In addition, the trilostane-induced reduction of serum aldosterone was compared to the reduction of cortisol concentration. Changes in serum aldosterone concentration between normal dogs and dogs with PDH were also compared.

✕ SUMMARY:

Methods: Seventeen dogs with PDH were administered trilostane orally. Hemogram, serum biochemical analyses, and adrenocorticotrophic hormone (ACTH) stimulation test for changes in serum cortisol and aldosterone were performed on each dog and re-evaluated four times after treatment began: at one, 3-4, 6-8, and 10-12 weeks. Twelve normal dogs were evaluated once.

Results: Baseline serum aldosterone concentrations did not change significantly after trilostane treatment began. Post-ACTH serum aldosterone concentrations were significantly decreased by trilostane

and median serum potassium concentration increased slightly. The greatest increase in median serum potassium concentrations occurred after the first week of treatment. However, the suppression of aldosterone synthesis was less severe than the suppression of cortisol synthesis. Serum aldosterone concentrations before and after ACTH stimulation were higher in dogs with PDH than in normal dogs.

Conclusions: Trilostane does not suppress aldosterone synthesis as much as it does cortisol synthesis.

🌀 CLINICAL IMPACT:

The greater effect of trilostane on cortisol synthesis than aldosterone synthesis has been well established prior to this study. However, the results of this study demonstrated that ACTH-stimulated aldosterone concentrations decline and then partially rebound during trilostane treatment. Serum potassium concentration increases during trilostane treatment and then after the first week of treatment, partially rebounds toward more normal median levels. The effects of trilostane on aldosterone synthesis goes through some equilibration during treatment, possibly due to the potent direct stimuli on aldosterone secretion caused by hyperkalemia and hypotension. Caution is warranted in treating dogs with trilostane if they are hyperkalemic. If used to treat primary hyperaldosteronism, the required dosage would be much higher than that required to treat PDH, and the duration of suppressed aldosterone synthesis may be short-lived without progressively increasing the dosage.

Caution is warranted in treating dogs with trilostane if they are hyperkalemic.



Persistent Mullerian Duct Syndrome Causing Male Pseudohermaphroditism

Kuiper H, Wagner F, Drogemuller C, et al. Persistent Mullerian duct syndrome causing male pseudohermaphroditism in a mixed-breed dog. Vet Rec 2004;155:400-401.

► INTRODUCTION:

Background: During embryogenesis, both male and female internal genitalia are present. External genitalia are bipotential. If the gonads are genotypically male, testosterone and mullerian regression factor (MRF) are secreted. Testosterone, produced by the interstitial cells, is converted to dihydrotestosterone which stimulates the external genitalia to become phenotypically male. MRF, produced by the Sertoli cells, causes the mullerian ducts to regress, and it may play a role in the descent of the testes to the scrotum.

Failure to develop normal internal and external genitalia can cause discordant genotype and phenotype. For example, an individual with bilateral testes and internal or external female genitalia are referred to as a male pseudohermaphrodite.

Objectives: The purpose of this report was to describe the cause for male pseudohermaphroditism and persistent mullerian duct syndrome in a mixed breed dog.

✕ SUMMARY:

Case Report: A 2-year-old, mixed breed dog with ambiguous, male-like phenotype was presented with urolithiasis. Physical examination revealed bilateral cryptorchidism and a small, malformed penis with hypospadias. Radiographs of the penis showed a misshapen os penis.

During the cystotomy to remove the urinary calculi, a small uterus and intra-abdominal gonads were found and removed. Histologic examination determined the gonads to be exclusively testis. The diagnosis of pseudohermaphroditism was based on the findings of male gonads with female internal genitalia. The presence of a uterus in

a genotypic male was also consistent with the persistent mullerian duct syndrome.

The cause for pseudohermaphroditism was investigated. A karyotype, done on circulating lymphocytes, revealed a male dog normal genotype (78, XY). Polymerase chain reaction (PCR) for the Sex-Determining region Y chromosome (SRY) was positive.

Conclusions: The findings in this case were consistent with a diagnosis of persistent mullerian duct syndrome.



CLINICAL IMPACT:

Persistent mullerian duct syndrome is a recessive trait in miniature schnauzers. Many affected dogs are cryptorchid. Otherwise, the condition usually goes unrecognized until a cryptorchid testis develops a Sertoli cell tumor, feminization, and becomes ill from pyometra. MRF is apparently produced in affected dogs but is not able to effect the changes expected. The case reported here illustrates that mixed breed dogs can also be affected.

A small uterus and intra-abdominal testes were found and removed.

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 middle-aged and older 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, galactorrhoea.

Skin and hair: myxedema of 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, 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 a 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 8 concentrations: 0.1 mg, 0.2 mg, 0.3 mg, 0.4 mg, 0.5 mg, 0.6 mg, 0.7 mg and 0.8 mg in 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
 Australian Veterinary Journal
 Canadian Journal of Veterinary Research
 Canadian Veterinary Journal
 Domestic Animal Endocrinology
 Endocrinology
 European Journal of Endocrinology
 Journal of Veterinary Internal Medicine
 Journal of the American Animal Hospital Association
 Journal of Small Animal Practice
 Journal of the American Veterinary Medical Association
 Journal of Veterinary Diagnostic Investigation
 Journal of Veterinary Medical Science
 Journal of Veterinary Medicine, Series A
 Journal of Comparative Pathology
 Journal of Veterinary Pharmacology and Therapeutics
 New Zealand Veterinary Journal
 Research in Veterinary Science
 Veterinary Journal
 Veterinary Pathology
 Veterinary Record
 Veterinary Radiology & Ultrasound
 ... and more than 20 others

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