

SMALL ANIMAL CLINICAL ENDOCRINOLOGY

**Volume 16, Issue 1, 2006**

A compendium of leading articles in the field of veterinary endocrinology selected for the  
veterinary practitioner.

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- Oral desmopressin administration is an effective treatment for central diabetes insipidus in cats. *J Feline Med & Surg* 2005;7:333-339.
- A cat with trauma-induced diabetes insipidus failed to respond adequately to conjunctival administration of desmopressin but was controlled with twice daily subcutaneous injections of desmopressin. *Aust Vet J* 2005;83:732-735.
- There may be an association between hypothyroidism and cricopharyngeal achalasia in dogs. *J Sm Anim Pract* 2005;46:553-554.
- Pretreatment serum T<sub>4</sub> concentration is not useful in predicting which cats with hyperthyroidism will have significant echocardiographic abnormalities. *Vet Radiol & Ultrasound* 2005;46:506-513.
- Changes in serum parathyroid hormone concentration in cats with urethral obstruction are appropriate for serum phosphorus and ionized calcium concentrations. *Vet Emerg Crit Care* 2005;15:179-184.
- Renal insufficiency is uncommonly associated with primary hyperparathyroidism in dogs. *J Am Vet Med Assoc* 2005;227:576-761.
- Excessive vitamin D accidentally added to a commercial canine diet caused hypercalcemia in dogs ingesting the food. *J Sm Anim Pract* 2005;46:334-338.
- A kitten with vitamin D-dependent rickets, type 2, has been reported. *J Fel Med & Surg* 2005;7:307-311.
- Home monitoring of diabetic dog or cat blood glucose concentration is practical and simple for most owners. *Can Vet J* 2005;46:718-723.
- Diabetic dogs with cataracts have altered, less aqueous, precorneal tear film. *Vet Ophthalmol* 2005;8:215-224.
- Purified porcine insulin is safe and efficacious in dogs. *J Vet Intern Med* 2005;19:675-682.
- Hypoglycemia associated with sinus bradycardia and corrected by administration of intravenous glucose has been reported in a dog and a cat. *J Sm Anim Pract* 2005;46:445-448.
- Injection with various forms of compounded ACTH produce similar 60 minute responses in serum cortisol concentrations. *J Am Anim Hosp Assoc* 2005;41:368-372.

- The range of adrenocortical function test results in dogs with neoplasia is wide. *Vet Compar Oncol* 2005;3:194-202.
- Fatal anaphylaxis in a dog has been associated with a dexamethasone suppression test. *J Vet Emerg Crit Care* 2005;15:213-216.
- Serum 17  $\alpha$ -hydroxyprogesterone or corticosterone concentrations after ACTH stimulation can be elevated in dogs with nonadrenal neoplasia and no clinical signs of hyperadrenocorticism. *J Am Vet Med Assoc* 2005;227:1762-1767.
- When serum cortisol concentrations are not diagnostic of hyperadrenocorticism, serum 17  $\alpha$ -hydroxyprogesterone may be useful in confirming the disease. *J Am Vet Med Assoc* 2005;227:1095-1101.
- There is no significant difference in survival times of dogs with hyperadrenocorticism treated with mitotane and those treated with trilostane. *J Vet Intern Med* 2005;19:810-815.
- Pretreatment, elevated serum parathyroid hormone concentration decreases significantly with trilostane when managing hyperadrenocorticism. *J Sm Anim Pract* 2005;46:537-542.
- Trilostane treatment can lead to complete remission of the clinical signs of alopecia X without adverse effects. *J Am Anim Hosp Assoc* 2005;41:336-342.
- Repeated glucocorticoid administration to the external ear canal can cause suppression of the hypothalamic-pituitary-adrenal axis in dogs. *Endocrinol* 2005;146:3163-3171.

## Hypothalamic-Neurohypophyseal Disorders

### **Feline Central Diabetes Insipidus**

Aroch I, Mazaki-Tovi M, Shemesh O, et al. Central diabetes insipidus in five cats: clinical presentation, diagnosis and oral desmopressin therapy. J Fel Med Surg 2005;7:333-339.

#### INTRODUCTION:

**Background:** Diabetes insipidus is a deficiency of antidiuretic hormone (central diabetes insipidus) or its action (nephrogenic diabetes insipidus). Central diabetes insipidus is either congenital or acquired. Acquired central diabetes insipidus most often results from trauma or neoplasia. Deficiency of antidiuretic hormone (ADH) is treated with synthetic ADH, called desmopressin. Desmopressin may be administered in the conjunctiva, intranasally, subcutaneously, or orally. The effectiveness of oral desmopressin in cats with acquired central diabetes insipidus is not known.

**Objectives:** The purpose of this study was to describe five cats with central diabetes insipidus that were treated with oral desmopressin.

#### SUMMARY:

**Case Reports:** Five domestic short hair cats less than three years of age at the onset of clinical signs were diagnosed with central diabetes insipidus. Each had access to outdoors and either a prior history of trauma or presumed to have received head trauma. Clinical signs included polyuria, polydipsia, urinary bladder distention, and dehydration. Urine specific gravity was in the hyposthenuric range (1.003 to 1.006). Water deprivation test or ADH response test results were characteristic of central diabetes insipidus, i.e. failure to concentrate during water deprivation and concentration of urine in response to exogenous ADH administration. Oral desmopressin (25 to 50 µg, twice to three times per day) produced variable but effective results.

**Conclusions:** Orally administered desmopressin is a safe and effective means of managing central diabetes insipidus in cats.

#### CLINICAL IMPACT:

Desmopressin, like ADH, is a nonapeptide that is altered by digestion. If a high concentration is administered, a portion will survive digestion intact and effectively control central diabetes insipidus. The effective dosage when administered orally is approximately 10 times the required dose given intranasally or in the conjunctiva. The oral dose is about 100 times that of the injectable dose with equivalent effects. Fortunately, the pressor effects are 1/4000 that of vasopressin.

Some owners of cats with central diabetes insipidus may find oral administration of desmopressin preferable, despite variable absorption, frequent administration (three times per day), and high cost. Most owners will consider conjunctival drops with the nasal solution best. Intranasal administration is less tolerated by most cats, and absorption can be significantly reduced if nasal congestion is present.

**Note to the publisher- possible pull quote:** “Some owners of cats with central diabetes insipidus may find oral administration of desmopressin preferable”

## **Trauma-Induced Diabetes Insipidus**

Campbell FE, Bredhauer B. Trauma-induced central diabetes insipidus in a cat. *Aust Vet J* 2005;83:732-735.

### INTRODUCTION:

**Background:** Diabetes insipidus is diuresis caused by the lack of antidiuretic hormone (ADH) or the lack of ADH effectiveness. The acquired deficiency of ADH may be caused by hypothalamic diseases such as neoplasia or granulomas, but cranial trauma can also be a temporary or permanent cause of diabetes insipidus. Replacement ADH therapy is possible with desmopressin, administered subcutaneously, orally, intranasally, or as conjunctival drops.

**Objectives:** The purpose of this report was to describe a cat with trauma-induced central diabetes insipidus and the results of management with parenteral desmopressin.

### SUMMARY:

**Case Report:** A 1-year-old, castrated male, domestic short hair cat was presented with a history of polyuria. The polyuria began after a 20 foot fall from a balcony one month prior to presentation for diagnostic evaluations. Trauma-induced central diabetes insipidus was suspected based on the history and initial physical and laboratory findings of hyposthenuria (1.004), normal hemogram, and serum chemistries. Abdominal ultrasonogram was within normal limits.

Urine concentration did not improve (1.006) in response to water deprivation and 8% reduction in body weight, but urine concentration increased significantly (1.028) within four hours from desmopressin administration. Management was unsuccessful with conjunctival administration of desmopressin, but subcutaneous administration of desmopressin, 5 mg (see Clinical Impact below about an error in this dosage), twice per day, was effective for at least 17 months in controlling polyuria and compensatory polydipsia.

**Conclusions:** This is the first report of successful long-term management of central diabetes insipidus with parenteral administration of desmopressin in a cat

### CLINICAL IMPACT:

The dosage of desmopressin reported used was 5 mg, twice per day, subcutaneously. However, the safe and effective subcutaneous dose for cats is 0.5 to 5 µg, twice per day. The reported dosage was in error. The reason for the lack of effect of conjunctival administration was not given. The dosage reported for conjunctival administration was also in error as mg rather than µg.

The value of this report remains the successful twice per day administration of subcutaneous desmopressin for nearly 1½ years by an owner of a cat with central diabetes insipidus that did not respond to conjunctival administration. Conjunctival administration will remain the preferred route by most owners, but an effective alternative route of administration for owners is apparently subcutaneous injections.

**Note to the publisher- possible pull quote:** “an effective alternative route of administration for owners is apparently subcutaneous injections”

## **Hypothyroidism**

### **Cricopharyngeal Achalasia and Hypothyroidism**

Bruchim Y, Kushnir A, Shamir MH. L-thyroxine responsive cricopharyngeal achalasia associated with hypothyroidism in a dog. J Sm Anim Pract 2005;46:553-554.

#### **INTRODUCTION:**

**Background:** Cricopharyngeal achalasia is a disease characterized by failure of the upper esophageal sphincter to open during swallowing. It typically occurs in young dogs, and the etiology is unknown. However, transection of the pharyngeal branch of the vagus nerve reproduces achalasia.

Hypothyroidism can cause peripheral and central nervous system disease through a variety of mechanisms including metabolic effects on neuron function, nerve compression due to myxedema, and vascular complications including atherosclerosis. Cricopharyngeal achalasia has not previously been reported as a manifestation of hypothyroidism.

**Objectives:** The purpose of this case report was to describe a case of cricopharyngeal achalasia in a dog with hypothyroidism.

#### **SUMMARY:**

**Case Report:** An 8-year-old, male boxer was evaluated for an acute onset of repeated ineffective swallowing, dysphagia, regurgitation, and nasal reflux. Hind limb weakness had been noted one month previously in the dog. Paraparesis with normal spinal reflexes and deficits of conscious proprioception in both hind limbs was noted on examination. A barium swallow study performed under fluoroscopy showed normal prehension and bolus formation and failure of the upper esophageal sphincter to relax to allow the bolus into the esophagus, consistent with cricopharyngeal achalasia. Hypercholesterolemia was the only significant abnormality noted on complete blood count and biochemistries. Serum total T<sub>4</sub> was 0.01 µg/dl (reference range 1-4 µg/dl) and the serum thyroid stimulating hormone concentration was 0.402 ng/ml (reference range 0.02-0.4 ng/ml). Administration of levothyroxine resulted in improvement in the swallowing disorder beginning six days, with complete resolution of the swallowing disorder and paraparesis occurring after one month. The serum T<sub>4</sub> concentration was slightly above the reference range and the TSH was at the lower limit of the reference range after two months of levothyroxine administration. The dog was considered normal when evaluated one year after initial examination.

**Conclusions:** The dog of this report had cricopharyngeal achalasia secondary to hypothyroidism.

#### **CLINICAL IMPACT:**

Since thyroid supplementation was not withdrawn to confirm a recurrence of cricopharyngeal achalasia, it is inaccurate to state that the achalasia was "l-thyroxine responsive". Being associated with an event is not equivalent to being caused by the event. The failure to find another cause for the swallowing disorder and paraparesis and rapid response coinciding with thyroid hormone supplementation are suggestive of hypothyroidism as the cause of the neurologic abnormalities in this dog. It was not mentioned if other signs of hypothyroidism were present in this case, but the more common clinical signs such as dermatologic abnormalities, lethargy, and

weight gain are sometimes absent in dogs with neurologic manifestations of hypothyroidism. Other causes of transient neuropathy or cricopharyngeal injury may have caused achalasia with recovery coincidentally coinciding with thyroxine administration.

Hypothyroidism should be considered a potential cause of focal or generalized peripheral nerve disorders in dogs, and thyroid function tests should be considered in all cases without another apparent cause. However, further evidence is needed to state that hypothyroidism is a cause for cricopharyngeal achalasia.

**Note to the publisher- possible pull quote:** “Hypothyroidism should be considered a potential cause of focal or generalized peripheral nerve disorders in dogs”



## **Hyperthyroidism**

### **Echocardiographic Variables Before and After Radioiodine Treatment**

Weichselbaum RC, Feeney DA, Jessen CR. Relationship between selected echocardiographic variables before and after radioiodine treatment in 91 hyperthyroid cats. *Vet Radiol & Ultrasound* 2005;46:506-513.

#### **INTRODUCTION:**

**Background:** Hyperthyroidism affects the cardiovascular system by increasing tissue oxygen consumption, causing vasodilation, increasing blood volume, altering myocardial composition, and enhancing beta-adrenergic stimulation of the heart. Clinical manifestations of these effects include tachycardia, systemic arterial hypertension, heart murmurs, and left ventricular hypertrophy. It has been presumed that the cardiovascular alterations present in hyperthyroidism resolve following treatment, although little evidence to support this exists.

**Objectives:** This study was performed to evaluate the echocardiographic changes present in hyperthyroid cats and the changes that occur two to three months after radioiodine treatment of the hyperthyroidism.

#### **SUMMARY:**

**Methods:** Ninety-one cats with hyperthyroidism were studied before and eight to 11 weeks after radioiodine treatment (2.9 to 6 mCi <sup>131</sup>I) to resolve the hyperthyroidism. Two-dimensional and M-mode echocardiography and measurement of serum T<sub>4</sub> concentration were performed at both times. All cats that had antithyroid treatment with methimazole (administered to 31% of cats) withdrawn for a minimum of two weeks prior to initial study.

**Results:** Serum T<sub>4</sub> concentration at the post-treatment evaluation was normal in 68%, below reference range in 31%, and above the reference range in 1%. One or more pretreatment echocardiographic measurement was outside of a published reference range in 34 cats. There was considerable variation in changes of measurements when pretreatment and post-treatment measurements were compared. The most common abnormalities in hyperthyroid cats prior to treatment were increased left ventricular end-diastolic dimension (LVEDD), left ventricular end-systolic dimension (LVESD), left ventricular posterior wall at end diastole (LVWED), left ventricular posterior wall at end systole (LVWES), and interventricular septum at end systole (IVSES). However, more cats had LVEDD and LVESD above the reference range after radioiodine treatment compared with before treatment. There was a significant decrease in interventricular septum end diastole, IVSES, LVWED, LVWED, LVWES, and fractional shortening after radioiodine treatment. The aortic root maximum dimension and LVESD were significantly higher after radioiodine treatment. There was no consistent correlation between pretreatment T<sub>4</sub> concentration and echocardiographic findings.

**Conclusions:** Most hyperthyroid cats have mild echocardiographic abnormalities prior to treatment and that some abnormalities may emerge after radioiodine treatment.

#### **CLINICAL IMPACT:**

In general, the cardiovascular changes in hyperthyroid cats are mild and have few long-term consequences. Only a small percentage of cats (less than 10%) had changes that were considered

clinically relevant prior to treatment. In many of these cats the echocardiographic abnormalities normalized after treatment of hyperthyroidism. The variability inherent in repeated echocardiogram measurements, the high percentage of cats with biochemical hypothyroidism (30%) after treatment, and the relatively short time to follow-up study may have been the cause of the increased frequency of increased left ventricular size after treatment of hyperthyroidism. Echocardiography is not necessary for clinical evaluation of the vast majority of cats with hyperthyroidism.

**Note to the publisher- possible pull quote:** “There was no consistent correlation between pretreatment T<sub>4</sub> concentration and echocardiographic findings.”

## Calcium Metabolism

### **Parathyroid Hormone and Vitamin D in Cats with Urethral Obstruction**

Drobatz KJ, Ward C, Graham P, et al. Serum concentrations of parathyroid hormone and 25-OH vitamin D<sub>3</sub> in cats with urethral obstruction. J Vet Emerg Crit Care 2005;15:179-184.

#### INTRODUCTION:

**Background:** Urethral obstruction results in a number of metabolic abnormalities including azotemia, hyperphosphatemia, hyperkalemia, and metabolic acidosis. Hypocalcemia occurs frequently in these patients, and ionized calcium can be markedly reduced in some cases. The cause and clinical significance of these findings are not clear.

**Objectives:** The objective of this study was to attempt to understand the pathogenesis of hypocalcemia associated with urethral obstruction in cats.

#### SUMMARY:

**Methods:** Blood samples were obtained from 19 male cats with urethral obstruction prior to treatment. In addition to routine serum biochemistries, hematocrit, pH, pCO<sub>2</sub>, pO<sub>2</sub>, ionized calcium, and lactate were measured. Serum parathyroid hormone (PTH) and 25-hydroxyvitamin D concentrations were also measured on the same sample.

**Results:** Ionized calcium concentration was below the reference range in eight cats and was within the reference range in the remaining 11 cases. Serum PTH concentration was elevated in 12 cats including all with a low ionized calcium. The serum PTH concentration was significantly correlated with ionized calcium. In addition, PTH was correlated with total calcium, phosphorus, pH, sodium, potassium, bicarbonate, urea nitrogen, and creatinine concentrations. There was no statistically significant relationship between 25-hydroxyvitamin D and any of the other parameters measured.

**Conclusions:** Inadequate secretion of PTH is not the cause of the hypocalcemia in cats with urethral obstruction.

#### CLINICAL IMPACT:

The cause of the hypocalcemia associated with urethral obstruction is likely due to the combination of hyperphosphatemia, decreased production of calcitriol, and resistance of target tissues to the action of PTH. While the clinical importance of the hypocalcemia is not clear in most cases, severe hypocalcemia combined with other electrolyte disturbances could contribute abnormal myocardial conduction and contractility in some cases.

**Note to the publisher- possible pull quote:** “Inadequate secretion of PTH is not the cause of the hypocalcemia in cats with urethral obstruction.”

## **Hypercalcemia**

### **Clinical and Laboratory Findings of Primary Hyperparathyroidism**

Feldman EC, Hoar B, Pollard R, et al. Pretreatment clinical and laboratory findings in dogs with primary hyperparathyroidism: 210 cases (1987-2004). J Am Vet Med Assoc 2005;227:756-761.

#### **INTRODUCTION:**

**Background:** Primary hyperparathyroidism is an uncommon cause of hypercalcemia in dogs. It is primarily caused by a benign parathyroid gland adenoma, but sometimes results from parathyroid gland hyperplasia or carcinoma. Clinical signs are limited to those resulting from hypercalcemia its complications.

**Objectives:** The purpose of this study was to describe the clinical and laboratory abnormalities of primary hyperparathyroidism in a large number of dogs.

#### **SUMMARY:**

**Methods:** Records of 210 dogs with primary hyperparathyroidism were reviewed for signalment, clinical findings, clinicopathologic results, serum parathyroid hormone (PTH) concentrations, and findings on diagnostic imaging. Primary hyperparathyroidism was diagnosed if the serum total calcium was 12 mg/dl or more at least twice during a period exceeding 30 days, one or more parathyroid gland masses were found on cervical ultrasound or at surgery, histologic changes compatible with parathyroid gland adenoma, carcinoma, or hyperplasia in dogs that underwent surgery, and the hypercalcemia resolved within five days of treatment of primary hyperparathyroidism. In addition, other disorders causing hypercalcemia were excluded (renal failure, neoplasia, and other diseases) and no significant findings were noted on thoracic radiographs and abdominal radiographs or ultrasound. Comparisons were made to 200 age-matched control dogs without hyperparathyroidism.

**Results:** The mean age of dogs with primary hyperparathyroidism was 11.2 years and the mean body weight was 22.2 kg. Keeshonden were the most common breed affected, comprising 20% of the affected dogs. Eighty-eight (42%) of the dogs did not have clinical signs noted by owners, rather hypercalcemia was noted when the dogs were evaluated for unrelated problems, primarily testing related routine geriatric screening or testing prior to anesthesia for dentistry procedures. Clinical signs of hyperparathyroidism were most frequently (106 dogs) consistent with lower urinary tract inflammation, including stranguria, pollakiuria, and hematuria. Polyuria and polydipsia were reported in 48%, weakness in 46%, decreased activity in 43%, inappetence in 37%, weight loss in 18%, and vomiting in 13%. Physical examination was unremarkable in 71% of dogs, while muscle wasting, weakness, obesity, and thin body condition were each reported in less than 10% of cases.

The mean serum total calcium concentration was 14.5 mg/dl, and was more than 16 mg/dl in 18%. The mean plasma ionized calcium concentration was 1.71 (reference range 1.12-1.41 nmol/L). Serum phosphorus concentration was below the reference range in 136 and in the lower third of the reference range in 59 dogs. Blood urea nitrogen and creatinine concentrations were elevated in nine and seven dogs, respectively. The mean urine specific gravity was 1.012; it was less than 1.012 in 50, 1.008-1.012 in 75, and 1.013-1.020 in 70 dogs. Cystic calculi were either present or had recently been removed prior to presentation in 65 dogs. Bacteria were cultured in

61 dogs, 20 of which had cystic calculi. Serum PTH concentration was measured in 185 of the dogs. It was within the reference range in 73% and was elevated in 27% of dogs with primary hyperparathyroidism. Cervical ultrasonography, performed in 130 dogs, identified a single parathyroid mass in 116 and bilateral masses in 13 dogs, while no mass was noted in the remaining dog.

**Conclusions:** Cystic calculi and urinary tract infections occur frequently in dogs with primary hyperparathyroidism.

CLINICAL IMPACT:

Most dogs in this study of primary hyperparathyroidism (73%) had serum PTH concentrations within normal range, but were inappropriate for the serum calcium concentration. All dogs had hypercalcemia which should have suppressed PTH concentration below normal. However, PTH secretion is regulated by ionized calcium concentration, and 9% of the dogs in this study diagnosed with hyperparathyroidism did not have elevated ionized serum calcium concentration, when measured. These were attributed to sample handling techniques. If serum PTH and ionized serum calcium are within normal range, a diagnosis of hyperparathyroidism should be tentative until new samples are evaluated or a diagnosis is made by exploratory surgery of the parathyroid region. Possible enlargement of a parathyroid on ultrasonography is insufficient by itself to diagnosis hyperparathyroidism.

The high incidence of signs of lower urinary tract disease in dogs with primary hyperparathyroidism should lead to evaluation of serum chemistries, especially calcium concentration, in dogs with recurrent lower urinary signs. Renal failure was rare in this group of dogs despite the sometimes marked elevation of serum calcium concentration. Induced coexistent hypophosphatemia in most dogs with primary hyperparathyroidism reduces the risk of calcium nephropathy.

**Note to the publisher- possible pull quote:** “evaluation of serum chemistries, especially calcium concentration, (should be performed) in dogs with recurrent lower urinary signs.”

## **Hypervitaminosis D**

Mellanby RJ, Mee AP, Berry JL, et al. Hypercalcaemia in two dogs caused by excessive dietary supplementation of vitamin D. *J Sm Anim Pract* 2005;46:334-338.

### INTRODUCTION:

**Background:** Vitamin D is essential for the normal intestinal absorption of calcium and phosphorus. It also aids in mobilizing calcium from the bones and calcium resorption in the kidney. Although humans can synthesize vitamin D in the skin under the influence of ultraviolet light, dogs must obtain vitamin D in their diets to maintain adequate body stores. The principal serum forms of vitamin D are 1,25-dihydroxyvitamin D and its precursor, 25-hydroxyvitamin D.

Excessive dietary vitamin D can cause hypercalcemia and hyperphosphatemia with resulting mineralization of soft tissues and hypercalcemia nephropathy. Sources of excessive vitamin D in dogs are usually ingested rodenticides, dermatologic ointments containing vitamin D, or iatrogenic from treatment for hypoadrenocorticism or owner added dietary supplements.

Vitamin D is routinely added to commercial dog foods. Excessive vitamin D in commercial foods can occur from incorporating food stuffs already rich in vitamin D (fish oil) or adding excessive supplements in error.

**Objectives:** The aim of these two case reports was to describe the clinical effects in dogs that were unknowingly fed a commercial diet with excessive vitamin D.

### SUMMARY:

**Case Reports:** A 3-year-old, spayed female, border collie was presented with a history of lethargy, stiff gait, and polyuria and polydipsia for two weeks. The most significant laboratory finding on routine plasma chemistries was hypercalcemia (2.93 mmol/L; reference range of 2.3-2.8 mmol/L). Serum 25-hydroxyvitamin D and 1,25-dihydroxyvitamin D concentrations were elevated while plasma parathyroid hormone concentration was undetectable. Analysis of the dog's commercial hypoallergenic diet revealed excessive amounts of vitamin D. Treatment with bisphosphonates (sodium clodronate) and a change in diet with acceptable levels of vitamin D led to resolution of the hypercalcemia.

A 7-year-old, male, German shepherd dog was presented with similar clinical signs and history to the first case, including being fed the same commercial diet. In addition, bilateral carpal joint effusions were present. Plasma biochemistries revealed total and ionized hypercalcemia. Serum concentrations of 25-hydroxyvitamin D and 1,25-dihydroxyvitamin D were elevated. Treatment consisted of a new diet and prednisolone. Within 16 days after changing the diet, carpal joint effusions were gone and hypercalcemia had resolved.

**Conclusions:** This is the first report of a commercial diet having toxic concentrations of vitamin D and causing clinical disease in dogs.

### CLINICAL IMPACT:

Analysis of the diet in this report revealed over 100 times the labeled concentration of vitamin D. Such levels are rapidly toxic and slowly resolve after diet correction. Vitamin D is fat soluble and stored in the liver for weeks to months. Changing to a diet with correct levels of vitamin D is essential to recovery. The value of supplementary treatment with bisphosphonates or

prednisolone is unknown.

It is somewhat surprising that the dogs of this report did not suffer fatal calcium nephropathy. When it was faddish to feed cod liver oil to puppies and hypervitaminosis D would ensue, otherwise healthy appearing puppies would suddenly die from rapidly developed renal failure.

**Note to the publisher- possible pull quote:** “Analysis of the diet in this report revealed over 100 times the labeled concentration of vitamin D.”

## **Vitamin D-Dependent Rickets**

Tanner E, Langley-Hobbs SJ. Vitamin D-dependent rickets type 2 with characteristic radiographic changes in a 4-month-old kitten. *J Fel Med & Surg* 2005;7:307-311.

### INTRODUCTION:

**Background:** The various forms of vitamin D are not equipotent. The most biologically active form of vitamin D is 1,25-dihydroxyvitamin D which is formed from 25-hydroxyvitamin D in the kidney. In order for 1,25-dihydroxyvitamin D to normally effect its target organs and raise serum calcium concentrations it must have receptors.

Vitamin D-dependent rickets, type 2 is a recessive deficiency of 1,25-dihydroxyvitamin receptors, an end organ resistance. It is characterized by rachitic bone changes, hypocalcemia, and secondary hyperparathyroidism. Some humans with type 2, vitamin D-dependent rickets develop total alopecia.

**Objectives:** The purpose of this report was to describe clinical and laboratory findings, treatment, and treatment response in a kitten with type 2, vitamin D-dependent rickets.

### SUMMARY:

**Case Report:** A 4-month-old, female, domestic short hair kitten was presented with a history of kyphosis, swellings in the forelimbs, reluctance to jump, and inappetence. It was smaller than its three more active male littermates. All had been fed commercial kitten diet. Physical examination revealed painful bony enlargements of the carpi and stifles. Ambulation was stiff with a stilted gait. The kitten was small for its age but with normal proportions. Laboratory findings in comparison to that of one of its littermates revealed elevated serum alkaline phosphatase and low urea and phosphorus. Total serum calcium was within normal reference range. Radiographs were consistent with osteopenia and flared growth plates.

Clinical and laboratory findings were suggestive of rickets. Plasma insulin-like growth factor-1 and 25-hydroxyvitamin D concentrations were normal in the small kitten. However, plasma parathyroid hormone and 1,25-dihydroxyvitamin D concentrations were elevated and ionized calcium was depressed.

Vitamin D-dependent rickets, Type 2 was diagnosed on the basis of the laboratory findings. Calcium (calcium lactate and borogluconate) and vitamin D (D<sub>3</sub> and then calcitriol) were supplemented. Although appetite and mobility seemed to improve, serum ionized calcium concentration remained below normal range, its gait remained stilted, and it failed to grow or gain weight. The kitten died seven months after diagnosis. Necropsy was not possible.

**Conclusions:** This was a rare case of a kitten with type 2, vitamin D-dependent rickets.

### CLINICAL IMPACT:

Several mutations of the vitamin D receptor have been recognized. In some, binding to the receptor may be impaired. Others may have impaired binding of the receptor to DNA. There is a wide variability in severity of clinical signs and response to calcitriol. Humans without accompanying alopecia tend to respond better to treatment, and those with impaired receptor binding respond better than those with impaired binding of the receptor to DNA. Based on the poor response to calcitriol, the kitten of this report may have had a mutation in the DNA-binding domain region of the vitamin D receptor.



**Note to the publisher- possible pull quote:** “the kitten of this report may have had a mutation in the DNA-binding domain region of the vitamin D receptor”

## Diabetes Mellitus

### **Owners' Perception of Home Monitoring of Blood Glucose in Pets**

Van de Maele I, Rogier N, Daminet S. Retrospective study of owner's perception on home monitoring of blood glucose in diabetic dogs and cats. Can Vet J 2005;46:718-723.

#### INTRODUCTION:

**Background:** Assessment of control of blood glucose in animals with diabetes mellitus can be difficult. Clinical signs, physical examination, and serum fructosamine concentrations are very important considerations when assessing glycemic control, but many animals can benefit from measurement of serial blood glucose concentrations early in the management of the disease or when complications become apparent. Blood glucose curves performed in the clinic are prone to error induced by stress and inappetence during the test. It is presumed that testing performed at home would circumvent these problems.

**Objectives:** The purpose of this study was to evaluate the practicality and problems associated with measurement of blood glucose in the home by owners of diabetic animals.

#### SUMMARY:

**Methods:** Owners of seven dogs and two cats with diabetes mellitus were sent a questionnaire regarding monitoring blood glucose at home in their pets. All owners had been trained in measurement of blood glucose concentrations in their homes using a hand held glucometer. Blood samples were obtained by hypodermic needle or lancet puncture of the marginal ear vein. Blood glucose was measured prior to and every two hours after insulin administration for 12 to 24 hours by owners in their homes. The questionnaire contained questions regarding the pet's illness, the technique used to measure blood glucose, difficulties encountered during testing, reasons for any reluctance for initiating home glucose measurements, and any benefits that home monitoring provided.

**Results:** During initial use of home glucose monitoring, difficulties encountered by owners more than 50% of the time in two or more cases included need for help with restraint of the pet, more than a single puncture to obtain a blood sample due to resistance of the animal, insufficient size of blood droplet, and resistance of the pet. Other common problems included the need for multiple punctures due to technical problems and inadequate absorption of blood onto the test strip. Most of these decreased in frequency as owners and pets became more experienced. Five of the nine pet owners were initially reluctant to monitor glucose themselves because of fear of hurting their pet, four were adverse to obtaining blood samples, four were concerned about expense, and three considered the technique time consuming. All owners reported that they thought the monitoring helped in controlling the diabetes mellitus in their pet because of improved clinical signs and their active participation in the management. Two owners preferred to have glucose concentrations measured by their veterinarians because of the time commitment involved, and one of these was also afraid of harming his pet.

**Conclusions:** Home monitoring of blood glucose is a practical and simple technique for most owners of diabetic pets.

#### CLINICAL IMPACT:

Home monitoring of blood glucose can be readily accomplished provided the owner is sufficiently motivated, intelligent, and adequately trained, and the pet tolerates the procedure. Treatment monitoring can possibly be enhanced by home monitoring of blood glucose, but home management of diabetic pets should not be contingent on the owner being able or willing to take blood samples from their pet at home. Other means of monitoring diabetic pets can be used, and possible enhanced quality or quantity of life from home blood monitoring of diabetic pets has not yet been established.

Puncture of the marginal ear vein as used in the present study is likely to result in an adequate volume of blood for measurement more often than techniques that sample capillary blood from the pinnae. Inadequate droplet size may result in a falsely lowered glucose measurement. Consultation with a veterinarian regarding results of the blood glucose testing will continue to be necessary to make appropriate treatment recommendations.

**Note to the publisher- possible pull quote:** “enhanced quality or quantity of life from home blood monitoring of diabetic pets has not yet been established”

## **Keratoconjunctival Effects of Diabetes Mellitus**

Cullen CL, Ihle SL, Webb AA, et al. Keratoconjunctival effects of diabetes mellitus in dogs. *Vet Ophthalmol* 2005;8:215-224.

### INTRODUCTION:

**Background:** Cataract extraction is performed frequently in dogs with diabetes mellitus. Over half of humans with diabetes mellitus develop corneal lesions because degeneration of corneal nerves, abnormal tear film, decreased tear production, and infection. Decreased corneal sensitivity and increased incidence of postoperative ulcerative keratitis has been reported in diabetic dogs, and this could adversely affect recovery from cataract removal surgery.

**Objectives:** This study was performed to evaluate corneal sensitivity, tear production and quality, and conjunctival changes in dogs with diabetes mellitus and cataracts.

### SUMMARY:

**Methods:** Ophthalmic examinations, corneal sensitivity, Schirmer tear test, tear film break up time, tear glucose concentration, conjunctival cytology, and histopathology of conjunctival biopsies were compared in 15 normal dogs, 15 dogs with diabetes mellitus and cataracts, and 15 euglycemic dogs with cataracts.

**Results:** Corneal sensitivity and Schirmer tear tests were reduced in diabetic dogs compared with normal dogs but not euglycemic dogs with cataracts. Tear film break up times were shorter in diabetic dogs compared with normal dogs or euglycemic dogs with cataracts. Tear glucose was higher in diabetic dogs than the other groups. Conjunctival microflora cultures isolated one or more bacterial species in eyes of four diabetics, seven nondiabetic dogs with cataracts, and four normal dogs. Differences in conjunctival cytology between groups were not noted. Mild to moderate mononuclear and neutrophilic inflammation was present in conjunctival biopsies from diabetic dogs and 70% had epithelial dysplasia.. There was no significant difference in the goblet cell to epithelial cell ratio between groups, although four diabetic dogs had moderate or marked decreases in goblet cells. Glycemic control was good or fair in 11, excellent in three, and poor in one diabetic dog.

**Conclusions:** Diabetic dogs with cataracts have substantial differences in keratoconjunctival characteristics compared with normal dogs and nondiabetic dogs with cataracts.

### CLINICAL IMPACT:

Because diabetic dogs with cataracts often undergo surgery to remove the lens, deficiencies in tear production and composition can predispose them to ulcerative keratitis. Decreased corneal sensitivity in diabetic dogs also could contribute to an increase in risk of developing corneal disease. It seems unlikely that the alterations noted in the diabetic dogs of this study would be sufficient to lead to clinical problems without other predisposing factors that would negatively affect the cornea and conjunctiva.

**Note to the publisher- possible pull quote:** “Corneal sensitivity and Schirmer tear tests were reduced in diabetic dogs”

## **Purified Porcine Insulin**

Monroe WE, Laxton D, Fallin EA, et al. Efficacy and safety of a purified porcine insulin zinc suspension for managing diabetes mellitus in dogs. J Vet Intern Med 2005;19:675-682.

### INTRODUCTION:

**Background:** Virtually all diabetic dogs are insulin-dependent. With the advent of recombinant human insulin replacing animal origin insulins for the treatment of diabetes mellitus in humans, most diabetic dogs have been treated with human insulin. Human insulin structure differs from canine insulin structure, but human insulin is biologically active in dogs. Porcine insulin structure is believed to be identical to dogs. All human insulins are used as off-label in dogs. A porcine insulin has recently been approved for use in dogs.

**Objectives:** The purpose of this study was to evaluate purified porcine insulin zinc suspension for management of diabetes mellitus in dogs.

### SUMMARY:

**Methods:** After an initial stabilization period to determine individual insulin doses, 53 diabetic dogs were treated for 60 days. Twelve hour glucose curves were performed and means determined for the curves and nadirs prior to insulin administration, after the dose determination period, and 30 days and 60 days after being on the study dose of insulin. Presence of polyuria, polydipsia, and ketonuria was monitored at blood glucose curve evaluation time points. The initial dose of insulin used was 1 U/kg, once per day. Any commercial diet acceptable to individual dogs was permitted.

Efficacy of treatment was assessed by blood glucose curves, physical examination findings, patient history, and presence and degree of polyuria, polydipsia, and ketonuria. Safety was based on results of a questionnaire, physical examination findings, hemogram, serum chemistries, and urinalysis.

**Results:** Means of the blood glucose curves and nadirs were significantly lower than the pretreatment means. The percentages of dogs with polyuria, polydipsia, and ketonuria were reduced by 82, 86, and 80%, respectively. After the initial stabilization and at the start of the 60 days of treatment, blood glucose concentrations were in normal range. After 30 days of treatment, the blood glucose concentrations were normal in 66%, and after 60 days of treatment, they were normal in 75%. At 60 days of treatment, 66% of the dogs required twice per day insulin injections. Some dogs experienced hypoglycemia during the study.

**Conclusions:** Purified porcine insulin zinc suspension is safe and efficacious for managing diabetes mellitus in dogs.

### CLINICAL IMPACT:

The results of this study demonstrated safety and efficacy of porcine insulin zinc suspension in management of diabetic dogs. However, there is no evidence that is it more efficacious or safer than other species' purified insulin suspensions.

The starting dose of 1 U/kg was near the mean maintenance dose for uncomplicated diabetics and as such too high for some of those below the mean requirement. This was evidenced by 21 of the 51 dogs started on that dose developing undesirably low blood glucose

concentrations and having subsequent dosage reduced. An appropriate starting dose should be 0.5 U/kg and titrated upward. Hyperglycemia for a few more hours or a few days is safer than hypoglycemia at any time.

It should be noted that most (66%) of the dogs eventually required twice per day injections. Twice per day dosage should be expected, but whenever once per day dosage can be used, it will increase the convenience and therefore the compliance of owners. The possibility of once per day injections should be considered and investigated in each diabetic dog, and proof of the need of twice per day injections expected in most.

**Note to the publisher- possible pull quote:** “ Purified porcine insulin zinc suspension is safe and efficacious for managing diabetes mellitus in dogs.”

## Hypoglycemia

### **Hypoglycemia and Bradycardia**

Little CJL. Hypoglycaemic bradycardia and circulatory collapse in a dog and a cat. J Sm Anim Pract 2005;46:445-448.

#### INTRODUCTION:

**Background:** Abnormally slowed heart rate can be from sinus bradycardia, from physiologic or pathologic factors outside the heart, or bradyarrhythmia, from pathologic factors within the heart. Hypoglycemia has been rarely associated with bradycardia in diabetic humans.

**Objectives:** The purpose of reporting this case was to describe the first published case of hypoglycemic bradycardia in animals.

#### SUMMARY:

**Case Reports:** Case 1 was a 9.5-year-old, castrated male, miniature schnauzer that was presented with diabetes mellitus which had been controlled for more than three years. Two weeks earlier, the dog had phacoemulsification surgery. The dog had been taken on an unusually long walk the day before it collapsed. Physical examination revealed bradycardia (55 bpm) and a prolonged capillary refill time. An electrocardiogram was consistent with sinus bradycardia. The principal laboratory finding was hypoglycemia (0.93 mmol/L). After administering intravenous glucose, the heart rate rose to normal (116 bpm). No other similar instances occurred in the next 2.5 years.

Case 2 was a 17-year-old, spayed female, domestic shorthaired cat with insulin-dependent diabetes mellitus. Recent to presentation for collapse, the cat had also been diagnosed with hyperthyroidism and placed on carbimazole and propranolol treatment. The morning of collapse the cat had eaten and then vomited. It was found collapsed later that morning. Examination revealed profound hypothermia and a heart rate of 80 bpm. Intravenous glucose administration was quickly followed by an increase in the heart rate. Within 10 minutes, the heart rate was 140-150 bpm. Propranolol was discontinued. No other similar incidences occurred in the next seven months, after which the cat died of renal failure.

**Conclusions:** Hypoglycemia may cause bradycardia and circulatory collapse in dogs and cats.

#### CLINICAL IMPACT:

These are two cases purported to be hypoglycemia-induced bradycardia. However, hypoglycemia from any cause is typically accompanied by tachycardia. The first insulin antagonist that is secreted in hypoglycemia is epinephrine which produces a rapid heart rate. The diabetic animals of this report were both being treated with insulin. Previous bouts with hypoglycemia can cause hypothalamic damage that impairs adrenergic response to developing hypoglycemia and might cause bradycardia, but neither of the cases reported here were said to have had severe previous hypoglycemic episodes.

A cause for hypoglycemia was not determined in the reported dog. As a result, the cause of the hypoglycemia may have independently caused bradycardia rather than hypoglycemia causing bradycardia. The author attributed the cause to hypoglycemia based on rapid improvement with intravenous glucose although cardiogenic shock had been diagnosed and volume expanding fluids were given in the same time period.

The hypoglycemic cat was on anti-thyroid medication and had hypothermia. Hypothermia can be caused by thyroid hormone deficiency and will cause bradycardia. Yet, the cat remained on carbimazole while it recovered. Beta-blockers, such as propranolol which the cat of this report was on when bradycardia was detected, block the normal response of epinephrine when hypoglycemia is developing resulting in more severe hypoglycemia occurring and will cause bradycardia. Again, the bradycardia was attributed to hypoglycemia because the cat improved after being administered glucose intravenously.

Since hypoglycemia does not normally cause bradycardia, another piece of this unusual pathogenesis must not have been identified yet. Previous hypothalamic damage from hypoglycemia is one possibility, but not supported by the case histories of the present cases.

**Note to the publisher- possible pull quote:** “hypoglycemia from any cause is typically accompanied by tachycardia”



## Tests of Adrenal Function

### **Compounded ACTH for Adrenal Function Testing**

Kemppainen RJ, Behrend EN, Busch KA. Use of compounded adrenocorticotrophic hormone (ACTH) for adrenal function testing in dogs. J Am Anim Hosp Assoc 2005;41:368-372.

#### INTRODUCTION:

**Background:** Several years ago, commercially prepared adrenocorticotrophic hormone (ACTH) gel was discontinued by its primary manufacturer. It was replaced by synthetic aqueous ACTH (cosyntropin) that has been evaluated extensively for use in dogs and cats. Unfortunately, the cost of cosyntropin has recently increased several fold. ACTH preparations can also be obtained from compounding pharmacies. Because sources of materials and formulations differ among compounding pharmacies, the effect of administration of these preparations on plasma cortisol may vary.

**Objectives:** The purpose of this study was to evaluate the ability of compounded ACTH preparations to stimulate increases in plasma cortisol.

#### SUMMARY:

**Methods:** Five healthy adult dogs were each administered cosyntropin and four compounded ACTH preparations obtained from compounding pharmacies at separate times with three to four day intervals between treatments. Blood samples were collected for measurement of cortisol before and 30, 60, 90, and 120 minutes after administration of cosyntropin (5 µg/kg, intravenously) or compounded ACTH preparation (2.2 units/kg, intramuscularly). Serum cortisol concentrations in response to cosyntropin were compared with those obtained after compound ACTH administration.

**Results:** Serum cortisol concentrations after all compounded ACTH preparations were similar to those after cosyntropin. At 90 and 120 minutes, serum cortisol was lower in two of the ACTH preparations compared with cosyntropin. Cortisol was significantly higher at 120 minutes with one ACTH preparation compared to with cosyntropin. The concentration of ACTH measured in each of the compounded preparations varied widely from 11 to 925 µg/ml.

**Conclusions:** When using compounded ACTH preparations, blood samples should be collected at least at one and two hours after administration for measurement of cortisol.

#### CLINICAL IMPACT:

Reference ranges for ACTH response tests are crucial for proper test interpretation. Use of different ACTH preparations and sampling at different times might result in cortisol concentrations that are sufficiently different to be interpreted differently. The study did not include comparison of different lots of the ACTH preparations from each pharmacy, so the consistency of the activity of the drugs is not known.

**Note to the publisher- possible pull quote:** “When using compounded ACTH preparations, blood samples should be collected at least one and two hours”

## **Adrenocortical Function Associated with Neoplasia**

Boozer AL, Behrend EN, Kemppainen RJ, et al. Pituitary-adrenal axis function in dogs with neoplasia. *Vet Compar Oncol* 2005;3:194-202.

### INTRODUCTION:

**Background:** The stress of neoplasia can stimulate the pituitary-adrenal axis. Increased cortisol production may increase the morbidity of some hematopoietic neoplasias and provide a prognostic indicator for neoplasia.

**Objectives:** The purpose of this study was to assess the pituitary-adrenal axis in dogs with lymphoma and non-hematopoietic neoplasia with adrenocorticotrophic hormone (ACTH) stimulation testing, endogenous ACTH concentrations, and adrenal ultrasonography.

### SUMMARY:

**Methods:** Twenty dogs with lymphoma, 15 dogs with non-hematopoietic neoplasia, and 16 healthy dogs had their pituitary-adrenal axis function assessed by ACTH stimulation testing effects on serum cortisol concentrations, endogenous plasma ACTH concentration, and adrenal ultrasonography. Tests were begun in tumor bearing dogs prior to treatment.

**Results:** No significant difference was found between basal or ACTH-stimulated plasma cortisol concentrations in dogs with neoplasia and those without neoplasia. No significant difference existed in endogenous plasma ACTH concentrations between dogs with lymphoma and dogs with non-hematopoietic neoplasia. However, basal serum cortisol concentrations were elevated in 15% of dogs with lymphoma and 20% of dogs with non-hematopoietic neoplasia. ACTH-stimulated serum cortisol concentrations were exaggerated in 5% of dogs with lymphoma and 7% of dogs with non-hematopoietic neoplasia. Endogenous plasma ACTH concentrations were elevated in 5% of dogs with lymphoma and in no dogs with non-hematopoietic neoplasia. The percentages of lymphoma dogs with abnormally decreased concentrations of serum basal cortisol concentrations, post-ACTH stimulation serum cortisol, and endogenous ACTH concentrations were 5%, 20%, and 10%, respectively and of dogs with non-hematopoietic neoplasia: 13%, 13%, and 7%, respectively. No significant difference existed between dogs with mild, moderate, or severe neoplastic disease in basal or ACTH-stimulated serum cortisol concentrations. Based on ultrasonography, five of 20 dogs with lymphoma and two of 15 dogs with non-hematopoietic neoplasia had enlarged adrenal glands.

**Conclusions:** The clinical significance of changes in the pituitary-adrenal axis associated with neoplasia need to be investigated further.

### CLINICAL IMPACT:

The findings of this study are a mixed group. Some dogs with neoplasia had evidence of secondary hypoadrenocorticism. If treated with prednisone as part of a chemotherapeutic protocol, dogs with secondary hypoadrenocorticism should show clinical improvement even if their neoplasia is unresponsive. Most lymphoma cases would show benefits of both lympholysis and glucocorticoid replacement.

Conversely, dogs with an appropriate stress response to neoplasia might be adversely affected by adding additional glucocorticoids in the form of prednisone chemotherapy. Adverse effects could include immunosuppression, osteopenia, and delayed healing time from tumor

excision. Similar studies on common single tumor types on subsets based on age, sex, tumor size, metastasis, and severity of disease are needed to determine the clinical significance of neoplasia effects on the pituitary-adrenal axis.

**Note to the publisher- possible pull quote:** “No significant difference was found between basal or ACTH-stimulated plasma cortisol concentrations in dogs with neoplasia and those without neoplasia.”

## **Dexamethasone Suppression Anaphylaxis**

Schaer M, Ginn PE, Hanel RM. A case of fatal anaphylaxis in a dog associated with a dexamethasone suppression test. J Vet Emerg Crit Care 2005;15:213-216.

### INTRODUCTION:

**Background:** Dexamethasone is a synthetic glucocorticoid commonly used to assess the normal feedback response on adrenocorticotrophic hormone (ACTH) secretion. Failure to suppress ACTH and as a result, decrease plasma cortisol concentration, with dexamethasone is suggestive of hyperadrenocorticism.

Type 1 hypersensitivities are mediated by immunologic lysis of mast cell membranes and sudden release of histamine and other vasoactive amines. Hypotension and edema (wheals) from vasodilation can result with the risk of anaphylactic shock and death. Antigens which trigger Type 1 hypersensitivities are various. The most common are proteins that are injected such as in stinging insect venom or vaccinations following a previous sensitizing event.

**Objectives:** The purpose of this report is to describe a fatality associated with the dexamethasone suppression test in a dog.

### SUMMARY:

**Case Report:** An 8-year-old, spayed female, cocker spaniel was presented to be evaluated for possible hyperadrenocorticism. Eight months earlier, the dog had been treated for immune-mediated thrombocytopenia with dexamethasone in polyethylene glycol and maintained afterward on prednisone. Seven months later, the dog had been presented with a ruptured anterior cruciate ligament. During the orthopedic exam, it was noted that the dog had a pendulous abdomen. Laboratory findings included an elevated serum alkaline phosphatase activity (1037 U/L). Urinalysis reveal isothermia and proteinuria. The dog was still on prednisone at 2.5 mg, every other day. Basal and post-ACTH stimulated serum cortisol concentrations were normal. The adrenal glands were within normal size limits based on ultrasonography. Prednisone administration was discontinued for five days, and the dog was returned for a dexamethasone suppression test.

High-dose (0.1 mg/kg) dexamethasone for testing suppression was administered intravenously. The total dose was 1.7 mg. The dog immediately collapsed, urinated, and went into coma. Soon after, cardiopulmonary arrest was confirmed. Despite extensive efforts at resuscitation, the dog died. Necropsy revealed normal adrenal changes and changes consistent with congestive heart failure and anaphylaxis.

**Conclusions:** This was the first case in the dog of dexamethasone-induced anaphylaxis.

### CLINICAL IMPACT:

Anaphylaxis was the probable cause for death in the dog of this report. Other causes for sudden cardiopulmonary arrest such as air embolism, toxins, or cardiac conduction lesions were ruled out by necropsy and examination of the dexamethasone solution for contaminants. The authors assumed that dexamethasone was the triggering antigen based primarily on the lack of polyethylene glycol-induced anaphylaxis reports in the dog. However, the only dexamethasone

product mentioned in this report was apparently the same that was given for thrombocytopenia and later for dexamethasone suppression testing. The major constituent of that dexamethasone solution is 500 mg/ml of polyethylene glycol. Although polyethylene glycol has not been reported to cause anaphylaxis in the dog, it is an established cause for anaphylaxis in humans. (See: Anaphylactic shock after oral intake and contact urticaria to polyethylene glycol. *Allergy* 2007;62:92-93). Sensitization to polyethylene glycol is more likely than to dexamethasone. Polyethylene glycol is a vehicle for skin, otic, and ophthalmic products as well as laxatives.

**Note to the publisher- possible pull quote:** “polyethylene glycol is an established cause for anaphylaxis in humans. ”

## Hyperadrenocorticism

### **Serum 17 $\alpha$ -Hydroxyprogesterone and Corticosterone Concentrations in Hyperadrenocorticism**

Behrend EN, Kemppainen RJ, Boozer AL, et al. Serum 17  $\alpha$ -hydroxyprogesterone and corticosterone concentrations in dogs with nonadrenal neoplasia and dogs with suspected hyperadrenocorticism. J Am Vet Med Assoc 2005;227:1762-1767.

#### INTRODUCTION:

**Background:** Diagnosis of hyperadrenocorticism in dogs is based on abnormal adrenal function tests in the presence of typical clinical abnormalities. Because no adrenal function test is accurate in all situations, alternatives to the standard measurements of cortisol on the ACTH response test and dexamethasone suppression test are being investigated. Measurement of non-cortisol adrenal steroids such as 17-hydroxyprogesterone during the ACTH response test have been investigated in a number of studies, with variable results. Corticosterone, another adrenal steroid hormone has yet to be evaluated as a useful test for hyperadrenocorticism.

**Objectives:** The objective of this study was to determine the effect of nonadrenal neoplasia and hyperadrenocorticism on serum 17-hydroxyprogesterone and corticosterone concentrations during ACTH response testing in dogs.

#### SUMMARY:

**Methods:** Serum 17-hydroxyprogesterone and corticosterone concentrations before and one hour after synthetic ACTH were determined in 16 normal dogs in order to establish a reference range, and in 35 dogs with neoplasia (20 with lymphoma and 15 with other non-adrenocortical tumors). In addition, these hormones were measured in sera of 127 dogs suspected of hyperadrenocorticism that were submitted to an endocrine diagnostic laboratory.

**Results:** Post-ACTH cortisol concentration was above the reference range in three (8%) dogs with neoplasia and 59 (47%) of the 127 dogs suspected of hyperadrenocorticism. The mean post-ACTH serum 17-hydroxyprogesterone was significantly greater in dogs with neoplasia than normal dogs. The post-ACTH 17-hydroxyprogesterone concentration was above the reference range in 31% of all dogs with neoplasia and in 71% of the dogs with signs of hyperadrenocorticism that had an elevated post-ACTH serum cortisol concentration. The post-ACTH corticosterone concentration was not significantly different between normal dogs and the group with neoplasia. Post-ACTH corticosterone was above the reference range in eight (23%) of dogs with neoplasia and in 60% of dogs with signs of hyperadrenocorticism that had an elevated post-ACTH cortisol. The post-ACTH concentrations of 17-hydroxyprogesterone and corticosterone were directly correlated with post-ACTH cortisol concentrations.

**Conclusions:** Dogs with chronic illness, represented in this study by neoplasia, may have elevated serum cortisol concentration and more often elevated 17-hydroxyprogesterone and corticosterone concentrations without other evidence of hyperadrenocorticism.

#### CLINICAL IMPACT:

Similar to some other studies of 17-hydroxyprogesterone, it appears to be more susceptible to the effects of nonadrenal illness than does cortisol. Corticosterone also appeared to be elevated in

serum more often than cortisol in dogs with nonadrenal illness. False positive results using these parameters are common when testing dogs with chronic illness unrelated to hyperadrenocorticism. The study was not designed to evaluate the performance of 17-hydroxyprogesterone and corticosterone in cases of hyperadrenocorticism where cortisol was normal on an ACTH response test. Proper selection of cases for adrenal function testing by properly screening patient history, physical examination findings, and routine laboratory results is essential to accurately interpreting endocrine function tests.

**Note to the publisher- possible pull quote:** “17-hydroxyprogesterone appears to be more susceptible to the effects of nonadrenal illness than does cortisol”

## **Serum 17 $\alpha$ -Hydroxyprogesterone After ACTH Stimulation in Hyperadrenocorticism**

Benitah N, Feldman EC, Kass PH, et al. Evaluation of serum 17-hydroxyprogesterone concentration after administration of ACTH in dogs with hyperadrenocorticism. *J Am Vet Med Assoc* 2005;227:1095-1101.

### INTRODUCTION:

**Background:** Diagnosis of canine hyperadrenocorticism is complicated by the fact that no single test has perfect sensitivity or specificity. The ACTH response test is less frequently affected by nonadrenal illness than other screening tests such as the low-dose dexamethasone suppression test (LDDST) or urine cortisol:creatinine ratio. However, it is less sensitive than the LDDST, particularly when testing dogs with functional adrenal tumors. Recently, measurement of other adrenal steroid hormones has been utilized during the ACTH response test in attempt to increase the sensitivity of the test.

**Objectives:** The purpose of this study was to evaluate the utility of measurement of serum 17-hydroxyprogesterone in the diagnosis of hyperadrenocorticism in dogs.

### SUMMARY:

**Methods:** Dogs with suspected hyperadrenocorticism based on typical findings on history, physical examination, and routine laboratory tests were divided into three groups. Group 1 consisted of 40 dogs with pituitary-dependent hyperadrenocorticism (PDH) diagnosed by finding abnormal serum cortisol concentration on the LDDST or ACTH response test. Group 2 consisted of 12 dogs with adrenal tumors and abnormal results of LDDST. The five dogs in Group 3 had clinical findings consistent with hyperadrenocorticism but with normal cortisol responses on LDDST and ACTH response tests. All dogs in Groups 2 and 3 and 35 of 40 in Group 1 were tested with both the LDDST and the ACTH response test. Both serum cortisol and 17-hydroxyprogesterone were measured during the ACTH response test.

**Results:** The results of serum cortisol after ACTH-stimulation testing and dexamethasone suppression testing and 17-hydroxyprogesterone after ACTH-stimulation testing was diagnostic of hyperadrenocorticism in 79%, 93%, and 69% of dogs, respectively, with confirmed hyperadrenocorticism from either PDH or adrenal tumor. In dogs with PDH, the post-ACTH serum cortisol concentration was abnormal in 68% while the LDDST was abnormal in 89%. The serum 17-hydroxyprogesterone concentration was elevated in 68% of dogs with PDH as well, including nine dogs that had normal cortisol concentrations on the ACTH response test and two with a normal LDDST.

All 12 dogs with adrenal tumors had an abnormal LDDST while an elevated serum cortisol concentration on ACTH response testing was found in only four of 12. Elevated serum 17-hydroxyprogesterone concentration on ACTH response testing occurred in seven dogs with adrenal tumors. Of the five dogs with clinical findings consistent with hyperadrenocorticism with normal cortisol concentrations on LDDST and ACTH response testing, two had elevated serum 17-hydroxyprogesterone concentrations after ACTH. One of these two dogs was treated for hyperadrenocorticism with mitotane and had a good response. The remaining four dogs, including one with an elevated serum 17-hydroxyprogesterone concentration, were not treated for hyperadrenocorticism and further evaluation or follow-up was not performed.

**Conclusions:** Measurement of serum 17-hydroxyprogesterone concentration after ACTH



stimulation may be useful in a small percentage of cases where other adrenal function tests are equivocal.

CLINICAL IMPACT:

By definition, all dogs in this study with PDH had to have an abnormal adrenal function test result, so the post-ACTH serum 17-hydroxyprogesterone concentration could not have been more sensitive than the combination of post-ACTH serum cortisol concentration and LDDST. Not only could the sensitivity of the test not be established, the specificity was also not evaluated. This is important because another recent study of serum 17-hydroxyprogesterone measurements for assessing adrenal function found it was less specific than measurement of serum cortisol.

It appears that measurement of serum 17-hydroxyprogesterone concentration in conjunction with serum cortisol during an ACTH response test will increase the sensitivity of the test. However, the LDDST remains a more specific test, albeit more susceptible to false positive results.

**Note to the publisher- possible pull quote:** “ Measurement of serum 17-hydroxyprogesterone concentration after ACTH stimulation may be useful in a small percentage of cases where other adrenal function tests are equivocal.”

## **Survival Times for Hyperadrenocorticism after Mitotane and after Trilostane Treatments**

Barker EN, Campbell S, Tebb AJ, et al. A comparison of the survival times of dogs treated with mitotane or trilostane for pituitary-dependent hyperadrenocorticism. *J Vet Intern Med* 2005;19:810-815.

### INTRODUCTION:

**Background:** Trilostane is an adrenal steroid enzyme inhibitor that has proven to be an effective treatment for pituitary-dependent hyperadrenocorticism (PDH). The incidence of adverse effects due to trilostane is reported to be less than those associated with mitotane administration. Survival of dogs with PDH treated with mitotane has been reported to be about two years, but survival time for dogs treated with trilostane have not been published.

**Objectives:** The objective of this study was to determine if survival differs in dogs with PDH treated with trilostane or mitotane.

### SUMMARY:

**Methods:** A retrospective analysis of medical records at three referral clinics was performed. Inclusion criteria were a diagnosis of pituitary-dependent hyperadrenocorticism based on clinical signs, routine blood tests, adrenal function testing, and abdominal ultrasonography. Mitotane treatment consisted of standard induction protocol where mitotane was administered at 50 mg/kg daily until clinical signs improved and the post-ACTH cortisol concentration was less than 4.3  $\mu\text{g}/\text{dl}$ . Maintenance treatment with 50 mg/kg weekly was then administered. Treatment with trilostane was accomplished by once daily administration of 60 mg for dogs weighing 5-20 kg, 120 mg for those 20-40 kg, and 120 to 240 mg for dogs more than 40 kg. Dosage was adjusted to achieve control of clinical signs and in most cases a post-ACTH cortisol concentration of 1.4 to 4.3  $\mu\text{g}/\text{dl}$  four hours after trilostane administration. Breed, gender, weight, age, and date of death or loss to follow-up was recorded in all cases.

**Results:** Treatment varied among clinics, with one treating nearly equal numbers of dogs with trilostane and mitotane, one treating nearly all dogs with mitotane, and the third administered trilostane to all dogs. Overall, 25 dogs were treated with mitotane and 123 with trilostane. There was no significant difference in patient breed, age, weight, or reproductive status between the two treatments. Median survival of dogs treated with mitotane was 708 days while that of dogs administered trilostane was 662 days. There was no significant difference in survival between treatments. The fraction of dogs age at diagnosis and weight were negatively correlated with survival. Eighty-two of the 148 dogs died during the study. The cause of death was considered to be the result of PDH or its treatment in nine and could have been the result of PDH or its treatment in 14 dogs. The cause of death was unknown in 28 and not related to PDH or its treatment in 31 dogs.

**Conclusions:** Survival of dogs with PDH is similar when treated with mitotane or trilostane.

### CLINICAL IMPACT:

The survival times reported in this study are similar to those previously reported in dogs with PDH administered mitotane. Adverse effects of mitotane have been reported more often than those of trilostane, but suppression of cortisol secretion by mitotane is more effective, prolonged, and consistent than that induced by trilostane. These factors could also shorten survival.

Unfortunately, duration of survival of dogs with untreated PDH is unknown, so it is difficult to conclude the true efficacy of medical treatment of PDH.

**Note to the publisher- possible pull quote:** “Survival of dogs with PDH is similar when treated with mitotane or trilostane.”

## **Effects of Trilostane on Parathyroid Hormone, Calcium, and Phosphorus**

Tebb AJ, Artega A, Evans H, et al. Canine hyperadrenocorticism: effects of trilostane on parathyroid hormone, calcium, and phosphate concentrations. *J Sm Anim Pract* 2005;46:537-542.

### INTRODUCTION:

**Background:** Hyperadrenocorticism may be associated with increased parathyroid hormone (PTH) secretion and an increased risk of calcium uroliths, calcinosis cutis, peribronchial mineralization, and osteoporosis. Changes vary with species and with whether the cause of hyperadrenocorticism is iatrogenic or spontaneous.

**Objectives:** The objective of this study was to determine if treating hyperadrenocorticism affects PTH, calcium, or phosphate concentrations in dogs.

### SUMMARY:

**Methods:** Twenty-two dogs with spontaneous hyperadrenocorticism (16 pituitary-dependent, six adrenal-dependent) were analyzed for serum calcium, phosphate, and PTH concentration prior to initiating treatment with trilostane (1.5 mg/kg, once daily to 15 mg/kg, twice daily) and at a medium of 210 days during treatment. Twenty age and weight matched dogs without evidence of renal disease, hyperadrenocorticism, or corticosteroid administration were selected as controls from the hospital population.

**Results:** Dogs with hyperadrenocorticism had significantly higher serum PTH and phosphate concentrations than control dogs. Serum PTH concentrations after treatment with trilostane dropped to the same level as control dogs. Serum phosphate concentrations also declined significantly but not to the same level as control dogs. Although serum calcium concentrations were not significantly different than control dogs prior to trilostane therapy, concentrations of calcium increased significantly during trilostane therapy.

**Conclusions:** Hyperadrenocorticism in dogs causes secondary hyperparathyroidism because of calcium loss, phosphate retention, or both, which resolves with medical control of the hyperadrenocorticism.

### CLINICAL IMPACT:

Glucocorticoid excess appears to inhibit vitamin D-stimulated intestinal calcium transport. Declining serum ionized serum calcium stimulates PTH secretion while stabilizing serum calcium concentration. The net result is secondary hyperparathyroidism. Treatment that effectively controls serum cortisol concentrations should reduce pretreatment elevated serum PTH concentration by eliminating the inhibition of vitamin D effects.

The dogs with hyperadrenocorticism of this report were stated to have pretreatment hyperphosphatemia which is inconsistent with the expected effects of hypercortisolemia or elevated serum PTH concentrations. In fact, the mean pretreatment phosphorus of the control dogs and the dogs with hyperadrenocorticism were both within normal limits (1.11 and 1.75 mmol/L, respectively; reference for most laboratories, 0.9-2.0 mmol/L). The difference in serum phosphorus concentrations between control dogs and those with hyperadrenocorticism was the result of only a few outliers in the hyperadrenocorticism group. Diet or glucocorticoid-induced muscular catabolism may have contributed to the higher serum phosphorus concentrations of some dogs with hyperadrenocorticism. It is improbable that increased serum phosphorus was a

stimulus for secondary hyperparathyroidism in the dogs of this report with hyperadrenocorticism.

**Note to the publisher- possible pull quote:** “Hyperadrenocorticism in dogs causes secondary hyperparathyroidism”

## **Trilostane Treatment of Alopecia X**

Leone F, Cerundolo R, Vercelli A, et al. The use of trilostane for the treatment of alopecia X in Alaskan malamutes. *J Am Anim Hosp Assoc* 2005;41:336-342.

### INTRODUCTION:

**Background:** Alopecia X is an idiopathic nonpruritic bilateral hair loss syndrome primarily affecting young to middle-aged sled dogs. In Pomeranians and miniature poodles, it is suspected to be a tardive adrenocortical enzyme insufficiency. Suppression of adrenocortical activity with glucocorticoids (negative feedback on the pituitary), adrenocortical lysis with mitotane, or suppression of adrenocortical steroidogenesis by enzyme inhibition with trilostane are sometimes associated with improvement.

**Objectives:** The purpose of this group of case reports was to describe the successful management of Alopecia X in Alaskan malamutes with trilostane.

### SUMMARY:

**Case Reports:** Three male Alaskan malamutes from different home environments were presented with bilateral hair loss consistent with the diagnosis of Alopecia X. Laboratory findings included significantly elevated post-adrenocorticotrophic hormone (ACTH)-stimulated serum concentrations of 17-hydroxyprogesterone with normal serum concentrations of cortisol before and after ACTH stimulation and after dexamethasone suppression. One dog was castrated without any improvement occurring in the hair coat within a year post-surgery. A common male ancestor was present within five generations in all three dogs. The common male ancestor was present in both paternal and maternal lineage in one dog and twice in the paternal lineage of another dog.

Trilostane was administered at 3.0-3.6 mg/kg/day in a twice-daily divided dose for four to six months. Adrenocortical function suppression was monitored, and complete hair regrowth occurred in all dogs within six months with any apparent adverse effects.

**Conclusions:** Trilostane is a safe and effective treatment for Alopecia X in Alaskan malamutes.

### CLINICAL IMPACT:

Alopecia X is probably more than one disease. Reports of recovery have been attributed to castration or the administration of mitotane, growth hormone, or melatonin. Trilostane has now been added to the list of potential therapies. The source of the syndrome(s) has not been definitely determined and is complicated by the scarcity of cases and that spontaneous recovery can occur. Those that appear to respond to treatments may have incomplete or temporary response, or both.

However, the cases of this report had similar presentations and laboratory findings. In addition, they shared a common ancestor and responded to the same treatment. Trilostane may be the best treatment for Alopecia X in male Alaskan malamutes, but it may not be the best treatment for Alopecia X-like diseases in other breeds.

**Note to the publisher- possible pull quote:** “Trilostane may be the best treatment for Alopecia X in male Alaskan malamutes”

## **Hypoadrenocorticism**

### **Otic Glucocorticoid-Induced Secondary Hypoadrenocorticism**

Abraham G, Gottschalk J, Ungemach FR. Evidence for ototopical glucocorticoid-induced decrease in hypothalamic-pituitary-adrenal axis response and liver function. *Endocrinol* 2005;146:3163-3171.

#### **INTRODUCTION:**

**Background:** The adverse effects of the chronic administration of oral or injectable glucocorticoids in dogs are well known. The predominant adverse effects are hypothalamic-pituitary-axis suppression and adrenocortical atrophy and steroid hepatopathy. Chronic topical administration of glucocorticoids can also cause adverse effects, but the predominant form and extent of the risks are generally unknown.

**Objectives:** The purpose of this study was to determine if administration of an otic glucocorticoid preparation can suppress the hypothalamic-pituitary-axis and alter hepatic metabolism.

#### **SUMMARY:**

**Methods:** Ten clinically healthy beagles were administered an otic placebo for five days in their left ear canal. After the placebo run, 0.6 mg of topical otic dexamethasone was administered in their right ear canal, twice per day for 21 days. Plasma cortisol concentrations before and after adrenocorticotrophic hormone (ACTH)-stimulation were monitored prior to, during, and after administration of the otic dexamethasone. Hemograms and serum chemistry analyses were performed.

**Results:** Resting plasma cortisol and ACTH-stimulated cortisol concentrations were significantly suppressed within 11 days of beginning otic dexamethasone treatment and remained suppressed. At the same time, significant increases in serum activities of alkaline phosphatase, gamma-glutamyl transferase, alanine transaminase, and aspartate transaminase occurred. Hemograms revealed decreases in eosinophils and lymphocytes with an increase in neutrophils. A week after treatment was discontinued, plasma cortisol concentrations and hemograms returned to normal, but serum liver enzyme activities remained elevated.

**Conclusions:** Repeated applications of topical otic dexamethasone can be absorbed to sufficient extent to cause suppression of the hypothalamic-pituitary-adrenal axis, increases in liver serum enzyme activities, and stress-response alterations in the white cell differential count.

#### **CLINICAL IMPACT:**

The dogs in this study had intact epithelium in their external ear canals and were treated unilaterally. Still, the recommended administration of a commercial topical otic dexamethasone-containing product was capable of suppressing adrenocortical function, inducing a stress leukogram, and causing steroid hepatopathy in less than two weeks. Dogs with external otitis have inflamed external ear canals often with ulcerations. The degree of systemic absorption from topical otic glucocorticoids would be enhanced when treating clinical cases of external otitis with more profound adverse effects resulting than those that occurred in this study.

The risks of adverse effects of topical otic glucocorticoids can be minimized by irrigating the ear canals and the use of astringents to reduce systemic absorption from ulcers before

administering otic topical glucocorticoids. The frequency of administration and duration of treatment should be kept to a minimum. When possible the duration of treatment should be confined to less than two continuous weeks.

**Note to the publisher- possible pull quote:** “The degree of systemic absorption from topical otic glucocorticoids would be enhanced when treating clinical cases of external otitis”



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