

Diagnosis and management of naturally occurring hypoadrenocorticism in dogs

Carlos Melián DVM, PhD
Las Palmas, Spain

Mark E. Peterson DVM, DipACVIM
The Animal Medical Center, New York, USA



Mark E. Peterson is Head of the Department of Endocrinology at the Animal Medical Center, New York, NY, USA. Dr Carlos Melián worked with Dr Peterson before returning to Spain.

KEY POINTS

- Hypoadrenocorticism is rare in dogs, most commonly affecting young to middle-aged females; some breeds are at greater risk than others.
- Clinical signs are generally nonspecific and mimic more common diseases.
- Serum electrolyte disturbances of hyperkalemia and hyponatremia are characteristic of the disease, but concentrations may be normal in early or mild primary or secondary cases.
- Diagnosis is best confirmed by a low baseline serum cortisol concentration and a subnormal or negligible response to ACTH administration.
- Immediate treatment of acute adrenocortical insufficiency (Addisonian crisis) should include a large volume of IV isotonic fluids and a glucocorticoid.
- Long-term maintenance corticosteroid treatment generally consists of lifelong mineralocorticoid supplementation.

INTRODUCTION

Naturally occurring adrenocortical insufficiency, or hypoadrenocorticism, is uncommon in dogs. It is caused by deficient adrenal secretion of mineralocorticoids or glucocorticoids (usually both) (1–3). Hypoadrenocorticism can be caused by destruction of the adrenal cortex (primary adrenocortical insufficiency; Addison's disease) or, less commonly, deficient pituitary corticotropin (ACTH) production (secondary adrenocortical insufficiency) (3, 4).

Primary adrenal insufficiency is characterized by inadequate secretion of both glucocorticoids and mineralocorticoids and is thought to be the end result of an immune-mediated destructive process (5). Other rare causes include primary or metastatic bilateral adrenal neoplasia, bilateral adrenocortical amyloidosis, bilateral hemorrhage or infarction of the adrenal vasculature, trauma, systemic fungal disease involving the adrenal cortices and bacterial infection (e.g., tuberculosis) (3).

Secondary hypoadrenocorticism, which is much less common than the primary form, results from inadequate pituitary secretion of ACTH, causing glucocorticoid deficiency (3, 4). Reduced secretion of corticotropin-releasing hormone by the hypothalamus may also cause secondary hypoadrenocorticism. In secondary adrenal insufficiency, mineralocorticoid secretion is usually preserved because ACTH has little trophic effect on mineralocorticoid production. In most dogs with naturally occurring hypoadrenocorticism, the cause is idiopathic, but destructive lesions (e.g., tumors) in the hypothalamus or pituitary gland, inflammation, or trauma may also be rare causes.

HISTORICAL AND CLINICAL FINDINGS

Naturally occurring hypoadrenocorticism (**Figure 1**) most commonly develops in young to middle-aged dogs (1, 3). Females are at greater risk than males of developing the disease, accounting for approximately 70% of affected dogs (4, 6). One study has found that the Great Dane, the Portuguese Water Dog, the Rottweiler, the Standard Poodle, the West Highland White Terrier, and the Wheaten Terrier are most likely to contract the disease (4).

Common historical and clinical signs seen in dogs with hypoadrenocorticism are listed in **Table 1** (4, 7). The duration of these signs varies: most dogs have chronic intermittent signs, while some are in an acute crisis on examination. The severity of the disease also varies greatly.

Most clinical signs of hypoadrenocorticism are not specific and are common to a wide variety of more prevalent diseases. However, a waxing and waning course of illness that is exacerbated by stress and responds to nonspecific treatment and supportive care



Figure 1

A 2-year-old female West Highland White terrier that presented in a state of collapse and extreme weakness. This dog had marked azotemia (urea nitrogen = 18.2 mmol/l), hyperkalemia (8.4 mmol/l), hyponatremia (124 mmol/l), and hypochloremia (90 mmol/l). In addition, the dog was also markedly hypoglycemic (serum glucose = 2.1 mmol/l), which probably contributed to the weakness.

Table 1
Historical and clinical findings in 267 dogs with hypoadrenocorticism*

Historical owner complaints	Number of dogs (%)
Lethargy/depression	248 (93%)
Anorexia/poor appetite	246 (92%)
Vomiting	205 (77%)
Weight loss	123 (41%)
Waxing/waning course of illness	108 (40%)
Diarrhea	106 (40%)
Previous response to treatment	94 (35%)
Shaking	77 (29%)
Polyuria/polydipsia	65 (24%)
<i>Physical examination findings</i>	
Depression	231 (87%)
Weakness	198 (74%)
Collapse	96 (36%)
Hypothermia (< 37.5°C)	94 (35%)
Slow capillary refill time	77 (29%)
Weak pulse	48 (18%)
Bradycardia (< 70 beats per minute)	48 (18%)
Melena	41 (15%)
Painful abdomen	28 (10%)

*Compiled from data in references 4 and 7.

Table 2
Common clinicopathological abnormalities in 267 dogs with hypoadrenocorticism*

Finding	Number of dogs
Hyperkalemia	251 (94%)
Hyponatremia	219 (82%)
Sodium:potassium ratio < 27	252 (94%)
Hypochloremia	123 (46%)
Hypercalcemia	77 (29%)
Azotemia	231 (87%)
High serum alanine aminotransferase (ALT)	85 (32%)
Hyperbilirubinemia	53 (20%)
Hypoglycemia	52 (19%)
Anemia	66 (25%)
Eosinophilia	56 (21%)
Lymphocytosis	24 (9%)
Urine specific gravity < 1.030 (in face of azotemia)	112 (42%)

*Compiled from data in references 4 and 7.

(parenteral fluids administration and cage rest) should raise suspicions of adrenocortical insufficiency (4, 7).

CLINICOPATHOLOGICAL ABNORMALITIES

Common serum biochemical abnormalities found in dogs with untreated primary hypoadrenocorticism include hyperkalemia, hyponatremia, hypochloremia, hypercalcemia, azotemia, and acidosis (Table 2) (4, 7). Abnormal serum electrolyte concentrations occur in the vast majority of dogs with primary hypoadrenocorticism, but a definitive diagnosis cannot be made solely on the basis of serum electrolyte disturbances since a number of other diseases, particularly renal and urinary tract problems, gastrointestinal disorders, and acidosis can cause hyperkalemia or hyponatremia (3, 8, 9). The azotemia associated with hypoadrenocorticism is typically prerenal in origin and usually resolves with adequate fluid replacement. Serum biochemical evaluation of dogs with secondary adrenal insufficiency is usually unremarkable, although hyponatremia and azotemia may be seen; however, hyperkalemia is not found since mineralocorticoid secretion is preserved (4, 6).

Occasionally, some dogs with primary hypoadrenocorticism have normal serum potassium and sodium concentrations (termed atypical hypoadrenocorticism), probably because the ongoing

cortical destruction initially affects the glucocorticoid-secreting layers of the adrenal cortex before mineralocorticoid secretion is substantially affected (10). Conversely, recent treatment may obscure alteration in serum electrolyte concentrations. Multiple blood samples over a few weeks may be necessary to demonstrate abnormal serum electrolyte concentration in some of these dogs.

The evaluation of blood gases in dogs with primary hypoadrenocorticism usually shows varying degrees of metabolic acidosis. Uncompensated metabolic acidosis is the most common form of acidosis in dogs with hypoadrenocorticism, occurring in approximately 40% of dogs (7). Nevertheless, compensated metabolic acidosis or a combination of metabolic acidosis and respiratory alkalosis are not uncommon.

Hematological evaluation may show mild to moderate nonregenerative, normocytic, normochromic anemia and the absence of a stress leukogram (4, 7). Urinalysis frequently shows a urine specific gravity below 1.030, even in the face of azotemia (4). The cause of this impaired urine concentrating ability in these dogs is not known, but medullary washout and impaired medullary blood flow are probably important factors.

ELECTROCARDIOGRAPHIC FINDINGS

Electrocardiographic evaluation should be performed in all dogs with bradycardia or marked hyperkalemia (> 6.5 mmol/l) on examination. Abnormalities of cardiac conduction may have life-threatening consequences for dogs with hypoadrenocorticism. The classic electrocardiographic findings associated with hyperkalemic





Figure 2

(a) Lead II ECG recorded from a 7-year-old, 18 kg, female, mixed-breed dog presenting with vomiting, diarrhea, and collapse. There is bradycardia (approximately 50 bpm) and lack of P-waves (atrial standstill). (b) Lead II ECG recorded from the same dog 2 hours after IV administration of normal saline and glucocorticoids. Note that the ECG has essentially normalized.

Paper speed, 50 mm/sec. 1 cm = 1 mV.

Courtesy of Dr Philip Fox.

myocardial toxicity include QRS prolongation, low R-wave amplitude, high T-wave amplitude, P-R interval prolongation and atrial standstill (Figure 2) (1, 3, 4, 7). However, these abnormalities often correlate poorly with serum potassium concentrations because of the interaction of other concurrent electrolyte abnormalities, metabolic acidosis, and azotemia (11).

RADIOGRAPHIC FINDINGS

Survey radiographic abnormalities are most likely to occur in dogs suffering from moderate to severe primary hypoadrenocorticism. Most of these untreated dogs have one or more radiographic abnormalities, including a small heart (microcardia), hypoperfusion of the cranial lobar pulmonary artery and caudal vena cava, and a small liver (Figure 3) (4, 6, 7). These findings are thought to be related to volume depletion and poor tissue perfusion. Each of these abnormalities occurs in one-third to one-half of dogs with hypoadrenocorticism (4, 6, 7). A transient megaesophagus that resolves with treatment of the adrenocortical insufficiency has also been reported, but this is extremely rare (4, 12).

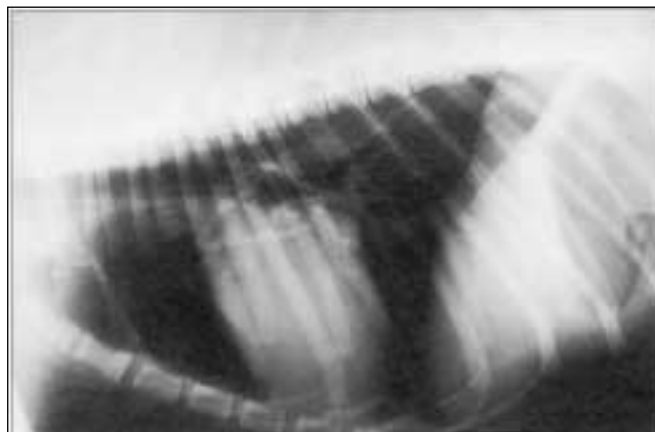


Figure 3 Left lateral radiograph of a 4-year-old mixed-breed female dog that was presented to the hospital in a shock-like state of secondary hypoadrenocorticism. Note the small heart. Also notice the reduced sizes of the caudal vena cava and pulmonary vessels, also caused by hypovolemia and poor cardiac output.

DIAGNOSIS

When the historical and clinicopathological evidence is consistent with hypoadrenocorticism, a finding of low-resting serum cortisol concentration coupled with a diminished or absent response to exogenous ACTH administration (post-ACTH plasma cortisol concentration < 50 nmol/l) confirms the diagnosis (1, 3, 4).

The ACTH stimulation test can be performed with either ACTH gel or synthetic ACTH (cosyntropin) preparations (13). When ACTH gel is used, the serum cortisol concentration is generally determined before and 2 hours after administration of ACTH (2.2 U/kg, IM) (1, 3). When synthetic ACTH is used, the serum cortisol concentration is determined before and 1 hour after administration of a total dose of 0.25 mg, IM or IV, regardless of the weight of the dog (1, 3). Recent work has shown that use of an ACTH dosage based on bodyweight (5 µg/kg, IV) yields similar results (14). With this low-dose protocol, one vial of ACTH can be used for more than one dog, especially when small-breed dogs are being tested.

If possible, the ACTH stimulation test should be completed before administration of glucocorticoids. Infusion of saline alone is usually sufficient initially while the test is being performed. Some dogs in life-threatening adrenal crisis need glucocorticoids without delay, before or during the ACTH stimulation test. In these dogs the ACTH stimulation test can be performed later and the test result will still be diagnostic. Dexamethasone is recommended for this initial treatment of acute adrenal crisis, because it is the only glucocorticoid preparation that does not cross-react with the serum

cortisol assays (15). Most glucocorticoids (prednisone, prednisolone, hydrocortisone, and cortisone) interfere with cortisol determination and falsely elevate the cortisol concentration. In dogs that have received these drugs, glucocorticoid supplementation should be changed to dexamethasone for at least 48–72 hours before the ACTH stimulation test is performed (15).

For interpretation of results of ACTH testing in hypoadrenocorticoïd dogs that have been given a single dose of glucocorticoids, the resting serum cortisol concentration is low, and the response to exogenous ACTH administration is diminished or absent (post-ACTH plasma cortisol concentration < 50 nmol/l). In dogs *without* hypoadrenocorticism treated with a single large dose of glucocorticoid, the resting serum cortisol concentration is also low (secondary to suppression of ACTH and subsequently cortisol by the glucocorticoid), but normal adrenocortical responsiveness is maintained (post-ACTH plasma cortisol concentration > 150–200 nmol/l) (16).

The presence of serum electrolyte abnormalities (i.e., hyperkalemia and hyponatremia) along with subnormal cortisol response to ACTH indicates primary hypoadrenocorticism. It should be remembered, however, that some dogs with secondary hypoadrenocorticism develop hyponatremia. The plasma ACTH concentration should be used to differentiate primary from secondary hypoadrenocorticism in dogs with a normal serum potassium concentration. Dogs with primary adrenocortical failure have little negative feedback to the pituitary gland, which should result in a markedly high plasma ACTH concentration (generally > 50 pmol/l), whereas the plasma ACTH concentration is low to

undetectable in dogs with secondary hypoadrenocorticism (3, 17, 18).

Samples for plasma ACTH determination should be drawn before corticosteroid administration to ensure accurate results. One major problem with determining plasma ACTH concentrations is the recommended procedure for handling samples (i.e., plasma is centrifuged and frozen immediately, packed in dry ice, and sent by overnight delivery service to the laboratory), which can be difficult for practitioners (3). However, the addition of a protease inhibitor (aprotinin) to whole blood in ethylenediaminetetraacetic acid (EDTA) tubes prevents degradation of the ACTH, and samples so treated can be shipped packed in ice packs by two-day mail (19).

TREATMENT

Acute adrenocortical insufficiency

Acute adrenocortical insufficiency (Addisonian crisis) is a life-threatening emergency requiring immediate intervention (**Table 3**). If the history and clinical signs are compatible with acute hypoadrenocorticism, samples for complete blood count, serum biochemical analysis (including serum electrolyte concentration) and urinalysis should first be collected and appropriate treatment instituted without delay. Definitive diagnostic testing to confirm hypoadrenocorticism (i.e., ACTH stimulation testing) can be carried out during the time of initial treatment with saline; ideally, glucocorticoids are withheld until completion of the test (3, 15).

Fluid treatment

Rapid intravenous administration of a large volume of isotonic fluids, preferably normal saline (0.9% sodium chloride), is crucial in the treatment of dogs with adrenal crisis, since it helps correct hypovolemia, hyperkalemia, and acidosis (1, 3, 15). Circulating potassium concentrations are reduced both by simple dilution and by improved renal perfusion and glomerular filtration. Normal saline is the fluid of choice because it contains no potassium. Potassium-containing fluids are a relative contraindication but can be used in lieu of not administering fluids. Since lactated Ringer's solution contains a small amount of potassium (4 mmol/liter), its administration will decrease the circulating potassium concentration, but at a slower rate than would be achieved by normal saline (7).

An indwelling intravenous catheter should be placed in the jugular or cephalic vein, and 0.9% normal saline rapidly infused at a rate of 20–40 ml/kg/hour during the first 1–2 hours (15). For the remaining 24-hour period, the isotonic saline should be infused at a maintenance rate of approximately 60 ml/kg. The fluids are discontinued when hydration, urine output, serum electrolytes, and serum creatinine concentrations are restored to normal (usually after 48–72 hours of treatment).

Glucocorticoid treatment

Intravenous administration of a glucocorticoid is also essential for dogs in adrenal crisis. Rapid-acting glucocorticoid preparations such as dexamethasone sodium phosphate (0.5–2.0 mg/kg) or prednisolone sodium succinate (2–10 mg/kg) are preferred (15). If the ACTH stimulation test has not yet been performed or is in progress, however, dexamethasone should be given, because it is the only glucocorticoid preparation that does not cross-react with serum cortisol assays. The initial dose can be repeated 2–6 hours later, if necessary. Glucocorticoid supplementation is gradually reduced over the next 3–5 days to a maintenance dosage of prednisone or prednisolone (0.2 mg/kg/day) as the dog's condition improves. Glucocorticoid replacement should be given parenterally until oral medication can be tolerated without risk of vomiting.

Table 3

Treatment of dogs with acute hypoadrenocorticism (adrenal crisis)

Initial treatment

1. *Fluids*
 - a. Isotonic saline (0.9% sodium chloride), administered IV, 20–40 ml/kg/hour during the first 1–2 hours
2. *Glucocorticoids*
 - a. Dexamethasone, 0.5–2.0 mg/kg (preferably, give after completion of ACTH stimulation test)
 - b. Prednisolone, 2–10 mg/kg (give only after completion of ACTH stimulation test)
3. *Mineralocorticoids*
 - a. Desoxycorticosterone acetate (DOCA), if available
 - b. Fludrocortisone acetate, 0.01–0.02 mg/kg/day
 - c. Desoxycorticosterone pivalate (DOCP), 2.2 mg/kg, IM
4. *Bicarbonate*
 - a. Consider if metabolic acidosis is severe (pH < 7.15)
5. *Dextrose*
 - a. Add 2.5% to 5.0% dextrose solution to IV fluids, if hypoglycemic. Severe or symptomatic hypoglycemia should first be treated by a slow IV bolus of 50% dextrose (0.5–1.0 ml/kg)
6. *Insulin and dextrose*
 - a. Consider only if severe hyperkalemia (> 8.5 mmol/l) and life-threatening myocardial toxicity are present to rapidly lower serum potassium. Administer insulin IV at a dosage of 0.25–0.5 U/kg. Give glucose at 2–3 g per unit of insulin, half as an IV bolus and half added to the intravenous fluids over the 6–8 hours

Subsequent treatment

1. *Fluids*
 - a. Maintain until oral alimentation is possible
2. *Glucocorticoids*
 - a. Gradually reduce parenteral glucocorticoids over 2–3 days to a maintenance dosage of prednisone or prednisolone (0.2 mg/kg/day)
3. *Mineralocorticoids*
 - a. Fludrocortisone acetate, 0.01–0.02 mg/kg/day
 - b. Desoxycorticosterone pivalate (DOCP), 2.2 mg/kg, IM every 25–30 days

Mineralocorticoid treatment

Desoxycorticosterone acetate (DOCA) was an excellent, rapidly acting, parenteral mineralocorticoid preparation used to correct hyperkalemia in dogs with primary hypoadrenocorticism, but the drug is no longer available in some countries. However, its unavailability is of limited clinical significance in so much as administration of fluids and glucocorticoids alone will correct most life-threatening complications of hypoadrenocorticism (e.g., hyperkalemia, hypovolemia, hyponatremia, hypotension, hypochloremia, and azotemia) (4, 7, 15). Oral mineralocorticoid supplementation with the mineralocorticoid fludrocortisone acetate can be instituted once the dog is eating and no longer vomiting. Alternatively, desoxycorticosterone pivalate (DOCP), the other available mineralocorticoid preparation used for chronic treatment, can be administered as soon as the diagnosis is confirmed.

Treatment of acidosis

Mild to moderate metabolic acidosis is common in dogs in adrenal crisis and generally resolves with the administration of fluids and glucocorticoids. Although less common, severe metabolic acidosis (pH < 7.15) may also develop in dogs with adrenal crisis



and may require treatment with sodium bicarbonate solution. The total dose of bicarbonate can be calculated by the following formula: deficit in mmol = (bodyweight in kg) × (0.5) × (base deficit) (7, 20). Twenty-five percent of the calculated deficit is given in the fluids over the initial 6–8 hours, and the acid–base status is then re-evaluated. It is unusual for dogs with hypoadrenocorticism to require additional bicarbonate if fluid replacement is adequate (7).

Treatment of hypoglycemia

Mild to moderate hypoglycemia is relatively common in dogs with hypoadrenocorticism and can be treated by adding 2.5–5% dextrose solution to the fluids (15). Symptomatic hypoglycemia, usually associated with blood glucose concentrations below 2.5 mmol/l, should first be treated by a slow intravenous bolus of 0.5–1.0 ml/kg of 50% dextrose followed by an infusion of 2.5–5% dextrose to maintain normoglycemia.

Correction of severe hyperkalemia

The alteration of cardiac conduction associated with high serum potassium concentration can progress to ventricular fibrillation or asystole. Rapid intravenous administration of fluids is sufficient in most dogs with hypoadrenocorticism to lower the serum potassium concentration within 1–2 hours. However, if hyperkalemic myocardial toxicity is life-threatening, intravenous administration of insulin and glucose may be indicated. With this regimen, insulin is given at a dosage of 0.25–0.5 U/kg; glucose is given at 2–3 g per unit of insulin, half as an intravenous bolus and half added to the intravenous fluids over the next 6–8 hours (7, 15). Dogs undergoing this treatment should be monitored cautiously for signs of hypoglycemia since hypoadrenocorticism makes them extremely sensitive to the hypoglycemic action of insulin. The intravenous administration of glucocorticoid, as described, will help to minimize the development of severe hypoglycemia, especially if given before insulin administration. Continuous electrocardiographic monitoring is indicated until the electrocardiogram has returned to normal.

Long-term management

Most dogs with hypoadrenocorticism have chronic progressive disease. Generally they do not require the aggressive treatment needed in those with acute hypoadrenocorticism (adrenal crisis). However, parenteral fluids and glucocorticoids may be indicated in dogs with chronic hypoadrenocorticism, especially if azotemia, dehydration, or vomiting are present. Once these problems have resolved, maintenance treatment can be initiated. Similarly, in dogs recovering from acute adrenal crisis, maintenance treatment is instituted once the dog is stable and oral medication can be tolerated. In dogs with primary hypoadrenocorticism, maintenance corticosteroid treatment consists of lifelong mineralocorticoid supplementation, generally together with glucocorticoid replacement therapy (2, 3). Because mineralocorticoid secretion is generally preserved in dogs with secondary hypoadrenocorticism, daily glucocorticoid replacement treatment is all that is needed.

Mineralocorticoid replacement

Two alternatives are available for mineralocorticoid replacement, including oral administration of fludrocortisone acetate and monthly injections of DOCP. Fludrocortisone acetate is initiated at a dosage of 0.01–0.02 mg/kg/day (7, 21). The daily dosage is adjusted by between 0.05 and 0.1 mg increments as needed on the basis of serial electrolyte determinations (i.e., sodium and potassium). Initially, serum electrolyte concentrations should be monitored every week until values have stabilized within the reference range. Once this is achieved, rechecks consisting of history, physical examination, and determination of serum sodium, potassium, and creatinine should be

Table 4

Long-term treatment for dogs with hypoadrenocorticism

Primary hypoadrenocorticism (Addison's disease)

1. *Mineralocorticoids*
 - a. Fludrocortisone acetate, 0.01–0.02 mg/kg/day
 - b. Desoxycorticosterone pivalate (DOCP), 2.2 mg/kg, IM, every 25–30 days
 - c. Recheck every 1–2 weeks initially and adjust dosage as needed to maintain serum electrolytes and urea nitrogen within reference range
2. *Glucocorticoids*
 - a. Prednisone or prednisolone (0.2 mg/kg/day), up to a maximum of 5.0 mg/day
 - b. May have to reduce dosage or discontinue if polyuria and polydipsia develop
3. *Salt*

Secondary hypoadrenocorticism

1. *Glucocorticoids*
 - a. Prednisone or prednisolone (0.2 mg/kg/day), up to a maximum of 5.0 mg/day
 - b. May have to reduce dosage if polyuria and polydipsia develop

performed every month for the first 3–6 months and every 6 months thereafter.

The daily dose of fludrocortisone required to control the disease gradually increases in some dogs, probably as a result of continuing destruction of the adrenal gland or changes in absorption or metabolism of the drug. Most dogs need a final dosage of 0.02–0.03 mg/kg/day, and only a few can be controlled on a dosage of 0.01 mg/kg/day or less (7, 21). Adverse effects (usually polyuria and polydipsia), inadequate control of the disease despite normal or high dosages (relative resistance to the effects of fludrocortisone), or financial considerations (especially when treating large to giant, breed dogs) may necessitate a change from fludrocortisone to DOCP in some dogs (7, 21).

When choosing DOCP as a long-term mineralocorticoid replacement, an initial dosage of 2.2 mg/kg, intramuscularly or subcutaneously, should be given at approximately 4-week intervals (7, 21–23). Periodic rechecks are recommended when this drug is used. Ideally, serum electrolyte concentrations should be determined at 2, 3 and 4 weeks after administration to determine the efficacy of normalizing electrolyte concentrations and duration of action of the drug. Once serum electrolyte concentrations have stabilized, the drug concentration should be determined just before each injection and the dosage and frequency of DOCP administration adjusted as necessary. Although most dogs require the drug at 3–4-week intervals, a few dogs need injections every 2 weeks (21). In some dogs the disease can be controlled at a lower dosage, but this approach should control practically all dogs and obviates the need for the practitioner to incrementally raise the maintenance dosage of DOCP over the first 6–12 months of supplementation. No adverse effects (such as hypertension or sodium retention) have been reported with the standard dosage of 2.2 mg/kg per injection (24). Nevertheless, one can attempt to lower the monthly maintenance dosage, particularly if cost is a factor.

Glucocorticoid replacement

Oral glucocorticoid replacement should be provided for dogs with primary or secondary hypoadrenocorticism. The recommended dosage of prednisone or prednisolone for long-term management of hypoadrenocorticism is 0.2 mg/kg daily (7, 21). However, daily

glucocorticoid administration appears to be necessary in only about half the dogs with primary hypoadrenocorticism. So if signs of glucocorticoid excess develop, it is reasonable to taper the dosage to alternate days or attempt to discontinue glucocorticoids to determine whether mineralocorticoid replacement alone is sufficient for maintenance treatment. Nevertheless, glucocorticoid supplementation may still be needed during periods of stress such as illness, trauma, or surgery.

Sodium chloride

Supplementation with sodium chloride (salt) may be useful in treating dogs with hypoadrenocorticism because it may allow a lower dosage of mineralocorticoid. However, in one recent study, administration of salt did not appear to have a sparing effect on the mineralocorticoid dosages (21). Most dogs fed commercial diets receive adequate quantities of salt. Nevertheless, concurrent salt

supplementation may be useful in an occasional dog with primary hypoadrenocorticism, especially in those receiving large dosages of mineralocorticoid. Furthermore, salt supplementation is useful, as well as cost-effective, in the occasional dog that is normokalemic but persistently hyponatremic despite the administration of an appropriate mineralocorticoid dosage.

PROGNOSIS

Overall, the prognosis for dogs with hypoadrenocorticism receiving appropriate hormone replacement is excellent. The median survival time is approximately 5 years, and it is not affected by the type of mineralocorticoid replacement administered, the cause of hypoadrenocorticism, or signalment (21). With proper treatment, these dogs can lead normal lives, with few if any restrictions on their activity.

REFERENCES

- Hardy, R. M. Hypoadrenal gland disease. In: Ettinger S. J., Feldman E. C., eds. *Textbook of Veterinary Internal Medicine*, 4th ed. Philadelphia: Saunders, 1995: 1579–93.
- Kintzer, P. P., Peterson, M. E. Hypoadrenocorticism in dogs. In: Bonagura, J. D., Kirk, R. W., eds. *Current Veterinary Therapy XII*. Philadelphia: Saunders, 1995: 425–29.
- Feldman, E. C., Nelson, R. W. Hypoadrenocorticism (Addison's disease). In: *Canine and Feline Endocrinology and Reproduction*, 2nd ed. Philadelphia: Saunders, 1996: 266–306.
- Peterson, M. E., Kintzer, P. P. Pretreatment clinical and laboratory findings in dogs with hypoadrenocorticism: 225 cases (1979–1993). *Journal of the American Veterinary Medical Association* 1996; **208**: 85–91.
- Schaer, M. S., Riley, W. J., Buergelt, C. D., et al. Autoimmunity and Addison's disease in the dog. *Journal of the American Animal Hospital Association* 1986; **22**: 789–94.
- Melián, C., Stefanacci, J., Peterson, M. E., Kintzer, P. P. Radiographic findings in dogs with naturally-occurring primary hypoadrenocorticism. *Veterinary Radiology and Ultrasound*. In press.
- Melián, C., Peterson, M. E. Diagnosis and treatment of naturally occurring hypoadrenocorticism in 42 dogs. *Journal of Small Animal Practice* 1996; **37**: 268–75.
- Graves, T. K., Schall, W. D., Refsal, K., Nachreiner, R. F. Basal and ACTH-stimulated plasma aldosterone concentrations are normal or increased in dogs with trichuriasis-associated pseudohypoadrenocorticism. *Journal of Veterinary Internal Medicine* 1994; **8**: 287–89.
- DiBartola, S. P., Johnson, S. E., Davenport, D. J., et al. Clinicopathologic findings resembling hypoadrenocorticism in dogs with primary gastrointestinal disease. *Journal of the American Veterinary Medical Association* 1985; **187**: 60–63.
- Rogers, W., Straus, J., Chew, D. Atypical hypoadrenocorticism in three dogs. *Journal of the American Veterinary Medical Association* 1981; **179**: 155–58.
- Hariman, R. J., Chen, C. M. Effects of hyperkalaemia on sinus nodal function in dogs: sino-ventricular conduction. *Cardiovascular Research* 1983; **17**: 509–517.
- Whitley, N. T. Megaesophagus and glucocorticoid-deficient hypoadrenocorticism in a dog. *Journal of Small Animal Practice* 1995; **36**: 132–35.
- Feldman, E. C., Stabenfeldt, G. H., Farver, T. B., Addiego, L. A. Comparison of aqueous porcine ACTH with synthetic ACTH in adrenal stimulation tests of the female dog. *American Journal of Veterinary Research* 1982; **43**: 522–524.
- Peterson, M. E., Wallace, M. S., Kerl, M. E., Kempainen, R. J. Dose-response relation between plasma concentration of ACTH and cortisol after administration of incremental doses of cosyntropin for ACTH simulation testing in dogs. *Journal of Veterinary Internal Medicine* 1996; **10**: 186.
- Peterson, M. E. Endocrinological emergencies in the dog. In: Grunsell, C. S. G., Hill, F. W. G., Raw, M. E., eds. *The Veterinary Annual*. London: Wright, 1990; **1**: 242–53.
- Kempainen, R. J., Sartin, J. L., Peterson, M. E. Effects of single intravenously administered doses of dexamethasone on response to the adrenocorticotrophic hormone stimulation test in dogs. *American Journal of Veterinary Research* 1989; **50**: 1914–17.
- Peterson, M. E., Orth, D. N., Halmi, N. S., et al. Plasma immunoreactive proopiomelanocortin peptides and cortisol in normal dogs and dogs with Addison's disease and Cushing's syndrome: basal concentrations. *Endocrinology* 1986; **119**: 720–30.
- Peterson, M. E., Kempainen, R. J., Orth, D. N. Effects of synthetic ovine corticotropin-releasing hormone on plasma concentrations of immunoreactive adrenocorticotropin, alpha-melanocyte-stimulating hormone, and cortisol in dogs with naturally acquired adrenocortical insufficiency. *American Journal of Veterinary Research* 1992; **53**: 421–25.
- Kempainen, R. J., Clark, T. P., Peterson, M. E. Preservation effect of aprotinin on canine plasma immunoreactive adrenocorticotropin concentrations. *Domestic Animal Endocrinology* 1994; **11**: 355–62.
- DiBartola, S. P. Metabolic acidosis. In: DiBartola, S. P., ed. *Fluid Therapy in Small Animal Practice*, 4th ed. Philadelphia: Saunders, 1992: 216–43.
- Kintzer, P. P., Peterson, M. E. Treatment and long-term follow-up of 205 dogs with hypoadrenocorticism. *Journal of Veterinary Internal Medicine* 1997; **11**: 43–49.
- Lynn, R. C., Feldman, E. C., Nelson, R. W. Efficacy of microcrystalline desoxycorticosterone pivalate for treatment of hypoadrenocorticism in dogs. *Journal of the American Veterinary Medical Association* 1993; **202**: 392–96.
- McCabe, M. D., Feldman, E. C., Lynn, R. C., Kass, P. H. Subcutaneous administration of desoxycorticosterone pivalate for the treatment of canine hypoadrenocorticism. *Journal of the American Animal Hospital Association* 1995; **31**: 151–55.
- Kaplan, A. J., Peterson, M. E. Effect of desoxycorticosterone pivalate administration on blood pressure in dogs with primary hypoadrenocorticism. *Journal of the American Veterinary Medical Association* 1995; **206**: 327–331.

