CE

An In-Depth Look:

CANINE HYPOADRENOCORTICISM

Canine Hypoadrenocorticism: Diagnosis and Treatment*

Patty Lathan, VMD[a]
John Tyler, DVM, DACVIM
Mississippi State University

ABSTRACT:

In dogs, hypoadrenocorticism is an uncommon but potentially life-threatening disease. Presumptive diagnosis is based on history, clinical signs, and laboratory findings. An adrenocorticotropic hormone stimulation test is required for definitive diagnosis. Patients most commonly have a history of waxing and waning gastrointestinal disease. A sodium:potassium ratio of less than 27:1 is consistent with hypoadrenocorticism; however, several other common diagnostic differentials should be considered. Treatment of acute hypoadrenocorticism (i.e., addisonian crisis) begins with aggressive intravenous fluid therapy to correct hypovolemia and electrolyte and acid–base abnormalities. In cases of life-threatening hyperkalemia, administering dextrose and regular insulin, calcium gluconate, or sodium bicarbonate in addition to fluid therapy may be necessary. Dexamethasone should be administered to correct glucocorticoid deficiency. Maintenance therapy includes fludrocortisone or desoxycorticosterone pivalate and prednisone. The long-term prognosis is good if a timely and accurate diagnosis is made and patients are properly treated and monitored.

Hypoadrenocorticism (Addison's disease) is an uncommon disease in dogs. It is most commonly caused by bilateral destruction of the adrenal cortex (primary hypoadrenocorticism); lack of pituitary secretion of adrenocorticotropic hormone (ACTH) leads to secondary hypoadrenocorticism.[1] Primary canine hypoadrenocorticism is typified by deficiency of both mineralocorticoid (aldosterone) and glucocorticoid (cortisol) activity. Secondary hypoadrenocorticism is characterized by a lack of cortisol production. Dogs with hypoadrenocorticism most commonly present with signs referable to the gastrointestinal (GI) tract, including vomiting, diarrhea,

*A companion article on pathogenesis and clinical features appears on page 110.

Send comments/questions via email **compendium@medimedia.com**, fax **800-556-3288**, or web **CompendiumVet.com**

[a]Dr. Lathan is now affiliated with Purdue University.

Differential Diagnosis of Significant Hyperkalemia and/or Hyponatremia

- Hypoadrenocorticism[1–4,6]
- Renal and urinary tract disease (i.e., anuric renal failure, obstructive uropathy, uroabdomen)[6]
- Severe GI disease[a]
- Trichuriasis-associated pseudohypoadrenocorticism[8,a]
- Severe metabolic or respiratory acidosis[21]
- Peritoneal effusion[b]
- Chylothorax[c]
- Congestive heart failure[6]
- Pregnancy[9]
- Artifacts (i.e., erythrocyte lysis in Akitas, marked thrombocytosis, marked leukocytosis)

[a]DiBartola SP, Johnson SE, Davenport DJ, et al: Clinicopathologic findings resembling hypoadrenocorticism in dogs with primary GI disease. *JAVMA* 187:60–63, 1985.
[b]Bissett SA, Lamb M, Ward CR: Hyponatremia and hyperkalemia associated with peritoneal effusion in four cats. *JAVMA* 218:1590–1592, 2001.
[c]Willard MD, Fossum TW, Torrance A, Lippert A: Hyponatremia and hyperkalemia associated with idiopathic or experimentally induced chylothorax in four dogs. *JAVMA* 199:353–358, 1991.

and weight loss. These signs may wax and wane or be acute.[1–5] This article discusses the diagnosis and treatment of canine hypoadrenocorticism.

DIAGNOSIS

A diagnosis of hypoadrenocorticism is based on history, clinical signs, laboratory findings, and direct assessment of adrenocortical reserve. Patients with hypoadrenocorticism typically present with sodium (Na^+):potassium (K^+) ratios of less than 27:1; however, this finding is not pathognomonic for hypoadrenocorticism (and does not occur with atypical hypoadrenocorticism, as described later). A recent study suggested that markedly decreased (<15) Na^+:K^+ ratios are more specific for hypoadrenocorticism.[6] These classic electrolyte abnormalities are often the first objective diagnostic finding that prompts a clinician to consider hypoadrenocorticism as a cause of a patient's clinical signs. In our experience, the diagnosis of hypoadrenocorticism is most often missed because electrolytes, especially Na^+ and K^+, are not evaluated or not available in a veterinarian's standard in-house chemistry panel. Patients with chronic or intermittent GI signs or acute, severe GI illness should have serum Na^+ and K^+ levels checked. Electrolyte measurement is also indicated in patients with arrhythmias or that are in shock. In particular, measuring serum Na^+ and K^+ concentration is an immediate concern in hypovolemic or markedly dehydrated patients that are bradycardic or have an inappropriately normal heart rate.[7]

A brief list of diagnostic differentials for hyponatremia and hyperkalemia is included in the box on this page. Among these, renal and GI diseases cause clinical signs most similar to those in patients with hypoadrenocorticism. Animals with trichuriasis-associated pseudohypoadrenocorticism may also have historical, physical examination, and serum electrolyte findings suggestive of hypoadrenocorticism, so fecal examinations are indicated in all patients suspected of having hypoadrenocorticism.[8] More recently, concurrent hyponatremia and hyperkalemia was described in three pregnant greyhounds.[9]

Definitive diagnosis of hypoadrenocorticism can be made via an ACTH stimulation test, which evaluates the ability of the zona fasciculata and zona reticularis of the adrenal cortex to respond to a maximal stimulus to produce cortisol. Animals with hypoadrenocorticism do not have enough functional adrenal cortical tissue to respond appropriately. Sole measurement of a basal cortisol concentration is inadequate because it does not test adrenocortical reserve, and healthy animals and animals with other serious diseases may also have low basal cortisol levels.[1,10,11] Once a diagnosis of Addison's disease has been made, it is possible to distinguish between primary and secondary hypoadrenocorticism by measuring plasma ACTH concentrations (which are increased in primary hypoadrenocorticism and decreased in secondary hypoadrenocorticism).[2]

THE ACTH STIMULATION TEST

One ACTH stimulation test protocol involves administering 0.25 mg of synthetic ACTH (cosyntropin; Cortrosyn, Amphastar Pharmaceuticals) intravenously or intramuscularly after obtaining an initial blood sample. A second blood sample should be drawn 1 hour after ACTH is given (intravenously or intramuscularly). Samples should then be analyzed for cortisol content. A diagnosis can be confirmed by a post-ACTH plasma cortisol concentration less than 2 µg/dl.[1] We use a more recently published protocol of 5 µg/kg IV[12] (0.005 mg/kg; maximum dose: 0.25 mg/dog) because it is more economically feasible. This lower dose has been shown to produce results similar to the 0.25 mg/patient dose in normal dogs, although no published studies have tested its efficacy in diagnosing hypoadrenocorticism.[13] A reconstituted vial of cosyntropin can be refrigerated for

up to 3 weeks without losing potency[14] or stored frozen (–20°C [–4°F]) in plastic syringes for up to 6 months.[15]

Two commercially available corticotropic gel preparations (ACTH Purified Corticotrophin, Virbac Australia; HP Acthar Gel, Rhône-Poulenc Rorer Australia) have been shown to adequately stimulate the adrenal gland of healthy dogs compared with cosyntropin.[12] The recommended dose is 2.2 U/kg IM, with sample collection 2 hours later. However, the gel preparation (HP Acthar Gel, Questcor Pharmaceuticals, Inc. [5 ml vial, 80 U/ml: $1,000]) that is currently available in the United States is more expensive than Cortrosyn (0.25 mg/vial: $710/10 vials; prices as of June 2004). Less expensive, compounded formulations are also available. A recent pilot study using a compounded ACTH gel formulation[b] suggested that the studied compounded formulation may be useful in diagnosing hypoadrenocorticism.[13] However, formulations and reliability may vary between pharmacies. In addition, to our knowledge, no studies have explored the variation in efficacy between intravenous administration of cosyntropin and intramuscular administration of commercial or compounded ACTH gel in hypovolemic patients. Intuitively, there may be decreased absorption of intramuscular injections in hypovolemic patients suspected of having hypoadrenocorticism.

Fluid resuscitation helps correct hypovolemia as well as electrolyte and acid–base imbalances and is the first priority in stabilizing patients in addisonian crisis.

ATYPICAL HYPOADRENOCORTICISM

Most patients diagnosed with primary hypoadrenocorticism are hyperkalemic and hyponatremic, whereas patients with secondary hypoadrenocorticism do not have electrolyte abnormalities. However, a subset of patients with primary hypoadrenocorticism has been identified that does not have classic electrolyte abnormalities. These patients are described as having atypical hypoadrenocorticism. Patients with atypical hypoadrenocorticism lack only glucocorticoid activity. They generally present with nonspecific signs, such as chronic or intermittent lethargy, weakness, vomiting, diarrhea, anorexia, and weight loss. The classic electrolyte abnormalities are not present; however, the presence of hypoglycemia (symptomatic or asymptomatic), lymphocytosis, eosinophilia, or an inappropriately normal lymphocyte count in a moderately to severely ill patient should prompt consideration of atypical hypoadrenocorticism.[16–18] Less commonly, patients with hypoadrenocorticism may present with acute collapse or acute GI disease.[18] Clinicians should

[b]Hook's Apothecary: *Corticotropin for Injection.* Available at www.hooksrx.com; accessed January 2005.

highly suspect hypoadrenocorticism in patients with unexplained GI disease, hypoglycemia, or other vague illness. An ACTH stimulation test must be conducted to diagnose hypoadrenocorticism.[16–18] ACTH levels should be measured in patients suspected of having atypical hypoadrenocorticism to rule out secondary hypoadrenocorticism (low levels would be expected in patients with secondary hypoadrenocorticism). Although patients with atypical hypoadrenocorticism do not initially have electrolyte abnormalities, some develop them within days, months, or years and then require mineralocorticoid replacement.[16,17]

MANAGING AN ADDISONIAN CRISIS

The goals of emergency therapy for an addisonian crisis are to correct hypovolemia, electrolyte abnormalities (particularly hyperkalemia), hypoglycemia (if present), acid–base abnormalities, and glucocorticoid and mineralocorticoid deficiencies.[1,7] The first priority is to restore blood volume and adequate perfusion to the tissues; therefore, intravenous fluids should be administered rapidly. An intravenous catheter should be placed in the jugular or cephalic vein, and blood for initial analysis and an ACTH stimulation test presample should be collected. Fluids should be administered at an initial shock-dose rate of 90 ml/kg/hr, with patient reassessment every 15 to 20 minutes. The fluid rate should be decreased as signs of shock abate. Blood

If a dog begins to show GI signs (e.g., vomiting, diarrhea, and/or melena) while on maintenance therapy for hypoadrenocorticism, the dose of prednisone may need to be increased.

pressure measurements may be obtained to assess the severity of hypotension and response to therapy. The fluid of choice is 0.9% sodium chloride because, in addition to diluting the high potassium concentration and increasing renal perfusion and glomerular filtration, it helps correct hyponatremia and hypochloremia. Although potassium-containing fluids (e.g., lactated Ringer's solution, Normosol-R [Abbott Laboratories]) are not optimal, they should be administered if 0.9% saline is not available.[19]

If hypoglycemia is suspected or proven, 50% dextrose should be added to the fluids to produce a 5% dextrose solution.[1,7] For example, 110 ml of 50% dextrose would be added to a 1 L bag of 0.9% sodium chloride. However, 5% dextrose (D5W) should not be used alone for emergency volume expansion because dextrose is rapidly metabolized to carbon dioxide and water, creating a hypotonic fluid that is an ineffective means of intravascular volume expansion.[20]

To reiterate, fluid therapy is the primary priority in managing an addisonian crisis—perfusion should be restored and hyperkalemia corrected before

treating other abnormalities. Therefore, as both a diagnostic measure and to evaluate therapy, affected patients should be monitored by electrocardiography. Electrocardiographic changes associated with hyperkalemia include atrial standstill or absent P waves, an increased P–R interval, increased amplitude of T waves (positive or negative deflection), broadened QRS complexes, and bradycardia. Not all patients with severe hyperkalemia have electrocardiographic abnormalities.[1,7]

Specific therapy aimed at correcting serum potassium abnormalities is rarely needed. Even markedly elevated potassium concentrations are almost always sufficiently corrected by aggressive intravenous fluid administration. Appropriate fluid therapy results in intravascular volume expansion and dilution of potassium. Normalized renal perfusion results in an increased glomerular filtration rate and increased urinary potassium excretion. However, for life-threatening bradycardia or arrhythmias, specific treatment is indicated. A 10% solution of calcium gluconate can be given at a dose of 2 to 10 ml/dog IV[21] over 10 to 15 minutes to help protect the myocardium from the effects of hyperkalemia; the cardioprotective effects of calcium last for approximately 10 to 30 minutes.[22] The patient must be continuously monitored by electrocardiogram, and calcium administration must cease if new arrhythmias appear (i.e., a shortened Q–T interval) or the heart rate drops significantly. This is only an adjunctive treatment: It does not lower potassium levels and is merely cardioprotective. Therefore, primary therapy aimed at volume expansion and lowering blood potassium levels should be instituted in conjunction with calcium gluconate administration.[7,23]

Therapies designed to quickly lower blood potassium levels in patients with severe, life-threatening hyperkalemia include intravenous administration of regular insulin (0.55 to 1.1 U/kg) followed by glucose infusion (2 g dextrose per unit of insulin).[21] Insulin exerts its effect by driving potassium into cells; simultaneous administration of glucose and insulin takes effect within 15 to 30 minutes and lasts for several hours.[22] Patients should be maintained on an infusion of 5% dextrose in 0.9% saline to help prevent hypoglycemia. Frequent monitoring of blood glucose levels is mandatory if this protocol is used because fatal hypoglycemia can develop. Therefore, blood glucose levels should be monitored hourly (as needed) for 4 to 6 hours following insulin administration, and dextrose should be administered as necessary.

Bicarbonate therapy can also be used to correct severe hyperkalemia because increased blood pH causes intracellular hydrogen ions to exit cells in exchange for potassium, which shifts intracellularly.[1,7] In an emergency, 1 to 2 mEq/kg of bicarbonate can be administered slowly intravenously.[21,22] Bicarbonate should *not* be added to calcium-containing solutions such as lactated Ringer's solution because calcium may precipitate with bicarbonate.[19] In our experience, combined use of bicarbonate and intravenous insulin has never been necessary. Use of calcium, insulin, and bicarbonate is reserved for life-threatening hyperkalemia; appropriate fluid therapy is the cornerstone of treating hypoadrenocorticism and hyperkalemia.

The prognosis for a dog with Addison's disease is good if the owners and veterinarian provide consistent treatment and monitoring.

Mild acidosis is usually corrected with fluid therapy alone. However, if acidosis is severe (i.e., serum bicarbonate or total carbon dioxide concentration [TCO_2] <12 mEq/L or blood pH <7.1) and/or causing life-threatening arrhythmias, bicarbonate may be administered.[1] The dose of bicarbonate needed to increase a patient's serum bicarbonate concentration to 12 mEq/L can be calculated using the following formula:

$$0.3 \times \text{Body weight (kg)} \times \left(12 - \text{Bicarbonate ion } [HCO_3^-]\right) = \text{mEq } HCO_3^-$$

This formula, which we use, allows conservative correction of acidosis. Others recommend correction to 14 mEq/L, which can be achieved by changing "12" to "14" in the above equation.[24] Because blood bicarbonate levels are equivalent to bicarbonate concentrations in aerobic conditions, HCO_3^- may be changed to TCO_2.[25] The calculated dose may then be added to the fluids (but not calcium-containing solutions) and administered over 6 to 8 hours.[4] If measurement of TCO_2 or HCO_3^- is not available, a

bicarbonate dose of 2 mEq/kg may be given. Acid–base status should be reassessed following initial bicarbonate therapy (and before giving an additional dose) to ensure that over- or undercorrection does not occur.

Glucocorticoid deficiency can independently cause or contribute to dehydration and shock because lack of cortisol decreases vascular sensitivity to catecholamines. Thus glucocorticoid therapy should be instituted in combination with fluid therapy.[26] Dexamethasone solution or dexamethasone sodium phosphate (which is preferable because of its rapid onset of action) should be used because dexamethasone does not interfere with the ACTH stimulation test because it is not measured by the laboratory test for cortisol (prednisone and hydrocortisone are). The recommended intravenous dose of dexamethasone (0.3[10] to 5[7] mg/kg) varies widely, depending on the clinician and the patient's condition; however, we generally use 0.5 to 1 mg/kg IV. ACTH may then be administered to begin the ACTH stimulation test.[1]

Although mineralocorticoid supplementation during a suspected hypoadrenocorticism crisis has been recommended by some authors,[1,17] others (including us) believe that aggressive fluid therapy and corticosteroid administration are sufficient to stabilize electrolyte concentrations in acute hypoadrenocorticism patients.[10,27] To our knowledge, there have been no objective, evidence-based studies that prove an advantage to using mineralocorticoids during a canine hypoadrenocorticism crisis. Using desoxycorticosterone pivalate[1] (DOCP; Percorten-V, Novartis Animal Health) and hydrocortisone sodium succinate for mineralocorticoid supplementation during an addisonian crisis has been described.[28] Hydrocortisone sodium succinate also has glucocorticoid properties and interferes with the ACTH stimulation test, so it should not be given until after the post-ACTH administration blood sample has been obtained.

Because hypoadrenocorticism manifests in many ways, other symptomatic therapies may be indicated in patients with acute disease. For example, a dog experiencing severe GI blood loss (i.e., hematochezia and melena) and anemia may require a blood transfusion. GI protectants such as H_2-blockers and sucralfate may also be helpful in patients with GI ulceration. Because violation of the GI barrier and subsequent bacterial translocation are potential causes and/or sequelae of hematochezia and melena, broad-spectrum antibiotics are indicated in these cases.[29,30]

Following initial treatment, dogs should be monitored for response to therapy. Mental status, pulse rate and quality, heart rate, and capillary refill time should be evaluated. Fluid rates should be adjusted to correct dehydration and azotemia and keep up with maintenance requirements and ongoing losses. Electrolyte concentrations should be measured before fluid therapy is initiated (if possible), following initial fluid resuscitation and then every 1 to 2 hours as needed until the patient is hemodynamically stable and potassium levels are out of the life-threatening range (i.e., <6.5 mEq/L). Electrocardiography should also be used to monitor hyperkalemic patients with arrhythmias until the electrocardiogram normalizes. Electrolyte levels can then be measured every 6 to 12 hours as indicated by the patient's condition. Correction of hyponatremia should be limited to an increase of less than 25 mEq/L in the first 48 hours (or 10 mEq/L in the

first 24 hours if there is evidence of liver disease) to prevent neurologic damage.[31]

Within the first few hours, dogs treated with fluids and glucocorticoids usually show rapid improvement, often regaining the ability to stand and walk and showing interest in the outside world. The electrocardiogram and blood urea nitrogen concentrations should also begin to return to normal. This response is highly suggestive of hypoadrenocorticism because dogs with most other illnesses, such as GI, renal, and hepatic diseases, do not usually show as dramatic a reversal of signs and laboratory abnormalities.[1]

Fluid therapy should be maintained as needed for rehydration and replacement of ongoing fluid losses, and oral water and food administration should be initiated based on the clinical response of the patient. Intravenous dexamethasone injections (0.05 to 0.1 mg/kg bid or tid) should be given until oral prednisone can be tolerated. Prednisone should initially be given at about 0.1 to 0.22 mg/kg/day and adjusted to suit the physiologic needs of the individual.[1]

AFTER THE CRISIS: MAINTENANCE THERAPY

Mineralocorticoid supplementation is necessary for maintaining electrolyte balance in primary hypoadrenocorticism. Feldman and Nelson[1] recommend administering DOCP, a long-acting mineralocorticoid, immediately following completion of an ACTH stimulation test in dogs suspected of having hypoadrenocorticism. In dogs subsequently proven to have normal adrenocortical function, harmful side effects have not been noted following DOCP injection.[1] However, it is important to note that DOCP therapy is not immediately necessary in treating an addisonian crisis and it should never be used as a replacement for appropriate intravenous fluid therapy combined with glucocorticosteroid administration in these patients.[10]

Primary therapeutic use of DOCP is part of the long-term management of primary hypoadrenocorticism. The initial dose is 2.2 mg/kg every 25 days; it can be given intramuscularly or subcutaneously in well-hydrated patients.[32,33] Electrolyte levels should be evaluated 12 to 15 days after DOCP administration to monitor the drug's peak effect; dose adjustments should be made based on these findings. If potassium levels are high and sodium levels low at this point, the dose should be increased by 5% to 10% at its next administration. If the potassium level is low and sodium level is high, the dose should be decreased. Dose changes affect peak activity of the drug but do not affect duration of activity. Electrolyte levels should be checked again after 25 days to monitor the duration of efficacy. High potassium and/or low sodium concentrations indicate that the interval must be decreased by 1 day.

In a 1993 multicenter study[32] of the effects of DOCP on 60 dogs with hypoadrenocorticism, two dogs had signs consistent with an adrenal crisis before 25 days; one of these dogs was managed adequately with injections every 21 days, while the other was considered a treatment failure. Thus close monitoring at home is necessary after initiating DOCP therapy, and owners should be warned that an acute crisis is possible if the duration of action is shorter than anticipated in their dog. Therefore, additional electrolyte monitoring at day 21 may be warranted.

Following initial stabilization, the frequency of administration may sometimes be slowly lengthened to 26 to 30 days. A 1997 retrospective study by Kintzer and Peterson[34] suggested that lower doses of DOCP (a median of 1.7 mg/kg IM to as low as 1 mg/kg IM) are effective in treating most hypoadrenal patients, but initially using the manufacturer's recommended dose of 2.2 mg/kg IM usually eliminates the need to increase the dose. Furthermore, Feldman and Nelson[1] warn that using lower doses may be risky and may precipitate an addisonian crisis.

DOCP has no corticosteroid activity, so prednisone should be supplemented at physiologic doses (0.22 mg/kg/day PO initially, then tapered to effect). Polyuria and polydipsia are sometimes noted with concurrent DOCP and prednisone administration; tapering prednisone to the lowest effective dose usually ameliorates the problem.[1,32,33] However, in our experience, most patients receiving DOCP require some level of maintenance corticosteroid therapy.

Hypoadrenocortical dogs can also be maintained with fludrocortisone acetate. The drug is given orally at a dose of 0.02 mg/kg/day divided bid.[1] The dosage should be adjusted gradually (0.05 to 0.1 mg/day) until the optimum replacement dose is discovered (which is reflected by consistently normal or near-normal electrolyte levels). The dog should be rechecked weekly after the initial crisis until electrolyte levels stabilize and then two to three times annually. If mild hyponatremia and normokalemia are present, the patient's food may be lightly salted (to effect) instead of increasing the dose of fludrocortisone.[10] The dose of fludrocortisone usually needs to be incrementally increased for the first 6 to 12 months of therapy, but then it usually stabilizes. In a

Table 1. Cost Comparison of Mineralocorticoid Supplementation for a 75-lb (34-kg) Dog with Hypoadrenocorticism for 25 Days

Mineralocorticoid	Cost[a]
DOCP[b] (2.2 mg/kg IM)	$100[c]
Fludrocortisone (generic; 0.020 mg/kg/day PO, divided)	$117[d]
Fludrocortisone (generic; 0.0235 mg/kg/day PO, divided)	$134[d]

[a]Prices were valid through January 2005.
[b]Percorten-V, Novartis Animal Health.
[c]Client price from Purdue University.
[d]Retail price from www.walgreens.com.

1997 retrospective study[34] involving 205 dogs treated for hypoadrenocorticism, 190 dogs were initially treated with both fludrocortisone and prednisone. The median starting dose of fludrocortisone was 0.013 mg/kg, and the final median dose was 0.023 mg/kg.

Unlike DOCP, fludrocortisone has some glucocorticoid activity. Therefore, only 50% of dogs that receive fludrocortisone require additional prednisone supplementation.[1] If needed, the suggested dosage of prednisone is 0.22 mg/kg/day tapered to control clinical signs of hypocortisolism. The glucocorticoid property of fludrocortisone is often responsible for the most common side effects associated with the drug—polyuria and polydipsia. If a dog develops polyuria and polydipsia while receiving fludrocortisone, salt supplementation should first be eliminated and additional prednisone should be tapered and discontinued without causing signs of hypocortisolism (if possible). If these measures do not successfully eliminate polyuria and polydipsia, the dog should be switched from fludrocortisone to DOCP.[10,34] In the 1997 study already mentioned,[34] 54 dogs experienced polyuria and polydipsia, polyphagia, weight gain, or hair loss with fludrocortisone administration. Adverse effects resolved in most patients when salt and additional corticosteroid supplementation were discontinued; however, polyuria and polydipsia did not resolve in 10 of the patients until they were switched to DOCP. In addition to occasionally causing polyuria and polydipsia, the glucocorticoid activity of fludrocortisone can also cause mild to moderate asymptomatic elevations in liver enzymes.

Prices of mineralocorticoid supplementation are listed in Table 1. Prices for both the starting and median maintenance doses of fludrocortisone have been calculated, although the dose may actually be greater for an individual patient.[34] Lower prices for fludrocortisone can be found through the Internet; however, we do not have experience using these pharmacies.

Dogs treated with either DOCP or fludrocortisone need two to 10 times the physiologic dose of prednisone during stressful periods. Owners should be instructed on how much to give during these periods (including hospitalization for another ailment or surgery), and administration of parenteral steroids by clients during an emergency is an option.[10]

Decreased appetite, intermittent vomiting or diarrhea, weight loss, and lethargy are all common clinical signs indicating that a patient with hypoadrenocorticism may need to have its dose of prednisone increased (or prednisone added to the therapeutic regimen).[1,35] If these clinical signs are caused by glucocorticoid deficiency, they should resolve within 12 hours of adequate supplementation.

Because dogs with secondary or atypical hypoadrenocorticism are only corticosteroid deficient, only prednisone must be administered. The same protocol as that for corticosteroid administration in primary hypoadrenocorticism should be used. The physiologic dose of prednisone should be given and adjusted to produce a clinically normal patient. The dose must be increased during stressful periods or illness. Many patients with atypical hypoadrenocorticism require mineralocorticoid replacement within days or years of the initial diagnosis. Thus close observation by the owner and periodic monitoring of electrolyte levels are indicated.[16,17,34]

PROGNOSIS

After the initial crisis, patients with hypoadrenocorticism usually have an excellent prognosis for returning to a normal quality of life and for a normal life expectancy. These dogs generally die from causes unrelated to their hypoadrenocorticism.[34] Owners should be informed that, although the disease is treatable, they will be responsible for medicating their dog for the remainder of its life. It is imperative that they fully understand that patients with hypoadrenocorticism must receive medications on schedule and undergo periodic laboratory testing. Although appropriate treatment and therapeutic monitoring may initially seem expensive, treating a dog in addisonian crisis is even more costly.

REFERENCES

1. Feldman EC, Nelson RW: *Canine and Feline Endocrinology and Reproduction*, ed 3. Philadelphia, WB Saunders, 2003, pp 394–435.
2. Melian C, Peterson ME: Diagnosis and treatment of naturally occurring hypoadrenocorticism in 42 dogs. *J Small Anim Pract* 37:268–275, 1996.
3. Rakich PM, Lorenz MD: Clinical signs and laboratory abnormalities in 23 dogs with spontaneous hypoadrenocorticism. *JAAHA* 20:647–649, 1984.
4. Schaer M, Chen CL: A clinical survey of 48 dogs with adrenocortical hypofunction. *JAAHA* 19:443–452, 1983.
5. Peterson ME, Kintzer PP, Kass PH: Pretreatment clinical and laboratory findings in dogs with hypoadrenocorticism: 225 cases (1979–1993). *JAVMA* 208:85–91, 1996.
6. Roth L, Tyler RD: Evaluation of low sodium:potassium ratios in dogs. *J Vet Diagn Invest* 11:60–64, 1999.
7. Schaer M: The treatment of acute adrenocortical insufficiency in the dog. *J Vet Emerg Crit Care* 11:7–14, 2001.
8. Graves TK, Schal WD, Refsal K, Nachreiner RF: Basal and ACTH-stimulated plasma aldosterone concentrations are normal or increased in dogs with trichuriasis-associated pseudohypoadrenocorticism. *J Vet Intern Med* 8:287–289, 1994.
9. Schaer M, Halling KB, Collins KE, Grant DC: Combined hyponatremia and hyperkalemia mimicking acute hypoadrenocorticism in three pregnant dogs. *JAVMA* 218:897–899, 2001.
10. Reusch CE: Hypoadrenocorticism, in Ettinger SJ, Feldman EC (eds): *Textbook of Veterinary Internal Medicine*, ed 5. Philadelphia, WB Saunders, 2000, pp 1488–1499.
11. Guyton AC, Hall JE: *Textbook of Medical Physiology*, ed 9. Philadelphia, WB Saunders, 1996.
12. Watson A, Church DB, Emslie DR, Foster SF: Plasma cortisol responses to three corticotrophic preparations in normal dogs. *Aust Vet J* 76:255–257, 1998.
13. Hill K, Scott-Moncrieff JC, Moore G: ACTH stimulation testing: A review and a study comparing synthetic and compounded ACTH products. *Vet Med* 99:134–147, 2004.
14. Plumb DC: *Veterinary Drug Handbook*, ed 4. White Bear Lake, MN, PharmaVet Publishing, 2002, pp 215–216.
15. Frank LA, Oliver JW: Comparison of serum cortisol concentrations in clinically normal dogs after administration of freshly reconstituted versus reconstituted and stored frozen cosyntropin. *JAVMA* 212:1569–1571, 1998.
16. Sadek D, Schaer M: Atypical Addison's disease in the dog: A retrospective survey of 14 cases. *JAAHA* 32:159–163, 1996.
17. Rogers W, Straus J, Chew D: Atypical hypoadrenocorticism in three dogs. *JAVMA* 179:155–158, 1981.
18. Lifton SJ, King LG, Zerbe CA: Glucocorticoid deficient hypoadrenocorticism in dogs: 18 cases (1986–1995). *JAVMA* 209:2076–2081, 1996.
19. Grooters AM: Fluid therapy in endocrine and metabolic disorders, in DiBartola SP (ed): *Fluid Therapy in Small Animal Practice*, ed 2. Philadelphia, WB Saunders, 2000, pp 375–386.
20. DiBartola SP (ed): Introduction to fluid therapy. *Fluid Therapy in Small Animal Practice*, ed 2. Philadelphia, WB Saunders, 2000, pp 265–280.
21. DiBartola SP, de Morais HA: Disorders of potassium, in DiBartola SP (ed): *Fluid Therapy in Small Animal Practice*, ed 2. Philadelphia, WB Saunders, 2000, pp 83–107.
22. Willard MD: Disorders of potassium homeostasis. *Vet Clin North Am Small Anim Pract* 19:241–263, 1989.
23. Bistner SI, Ford RB, Raffe MR: *Kirk and Bistner's Handbook of Veterinary Procedures and Emergency Treatment*, ed 7. Philadelphia, WB Saunders, 2000.
24. Willard MD: Fluids, electrolytes, and acid–base therapy, in Boothe DM (ed): *Small Animal Clinical Pharmacology and Therapeutics*. Philadelphia, WB Saunders, 2001, p 88.
25. DiBartola SP, Green RA, de Morais HS, Willard MD: Electrolyte and acid–base disorders, in Willard MD, Tvedten H (eds): *Small Animal Clinical Diagnosis by Laboratory Methods*, ed 4. Philadelphia, WB Saunders, 2004, p 131.
26. Behrend EN, Kemppainen RJ: Glucocorticoid therapy. *Vet Clin North Am Small Anim Pract* 27:187–213, 1997.
27. Melendez LD: Hypoadrenocorticism, in Wingfield WE (ed): *Veterinary Emergency Medicine Secrets*, ed 2. Philadelphia, Hanley and Belfus, 2001, pp 299–303.
28. Church DB, Lamb WA, Emslie DR: Plasma cortisol concentrations in normal dogs given hydrocortisone sodium succinate. *Aust Vet J* 77:316–317, 1999.
29. Brady CA, Otto CM: Systemic inflammatory response syndrome, sepsis, and multiple organ dysfunction. *Vet Clin North Am Small Anim Pract* 31:1142–1162, 2001.
30. Bellhorn T, Macintire DK: Bacterial translocation. *Compend Contin Educ Pract Vet* 26:229–235, 2004.
31. Brady CA, Vite CH, Drobatz KJ: Severe neurologic sequelae in a dog after treatment of hypoadrenal crisis. *JAVMA* 215:222–225, 1999.
32. Lynn RC, Feldman EC, Nelson RW, et al: Efficacy of microcrystalline desoxycorticosterone pivalate for treatment of hypoadrenocorticism in dogs. *JAVMA* 202:392–396, 1993.
33. McCabe MD, Feldman EC, Lynn RC, Kass PH: Subcutaneous administration of desoxycorticosterone pivalate for the treatment of canine hypoadrenocorticism. *JAAHA* 31:151–155, 1995.
34. Kintzer PP, Peterson ME: Treatment and long-term follow-up of 205 dogs with hypoadrenocorticism. *J Vet Intern Med* 11:43–49, 1997.
35. Schaer M: Hypoadrenocorticism, in Kirk RW (ed): *Current Veterinary Therapy VII. Small Animal Practice*. Philadelphia, WB Saunders, 1980, pp 983–988.

ARTICLE #3 CE TEST

This article qualifies for 2 contact hours of continuing education credit from the Auburn University College of Veterinary Medicine. Subscribers may purchase individual CE tests or sign up for our annual CE program. Those who wish to apply this credit to fulfill state relicensure requirements should consult their respective state authorities regarding the applicability of this program. To participate, fill out the test form inserted at the end of this issue or take CE tests online and get real-time scores at ***CompendiumVet.com****.*

1. Definitive diagnosis of hypoadrenocorticism can be made via

a. the Na^+:K^+ ratio.
b. a low-dose dexamethasone suppression test.
c. a fecal examination.
d. an ACTH stimulation test.
e. a complete blood count.

2. Which of the following has not reportedly caused low Na^+:K^+ ratios?
a. tapeworm infection
b. hypoadrenocorticism
c. uroabdomen
d. metabolic acidosis
e. peritoneal effusions

3. Which steroid does not interfere with the ACTH stimulation test?
a. prednisone
b. dexamethasone sodium phosphate
c. hydrocortisone
d. methylprednisone succinate
e. methylprednisone acetate

4. What is the first priority in stabilizing a dog in addisonian crisis?
a. steroid supplementation
b. fluid resuscitation
c. correcting acid–base abnormalities
d. correcting moderate hyperkalemia
e. insulin administration

5. Which treatment regimen is not acceptable as initial maintenance therapy for a dog with classic primary hypoadrenocorticism that is not in crisis at presentation?
a. prednisone alone
b. DOCP and prednisone
c. fludrocortisone alone
d. fludrocortisone and prednisone
e. fludrocortisone and dietary salt supplementation

6. Which patient has clinical signs and/or laboratory findings consistent with atypical hypoadrenocorticism?
a. a 2-year-old, spayed dog that occasionally has hypoglycemic seizures but is normal otherwise
b. a 10-year-old, intact male dog with chronic, intermittent vomiting and diarrhea
c. a 14-month-old, intact female dog with a 4-week history of intermittent vomiting and diarrhea but normal electrolyte concentrations
d. a 1-year-old standard poodle with vomiting and mild hyperkalemia but normal sodium concentrations
e. all of the above

7. Which treatment is not appropriate for severe hyperkalemia?
a. aggressive fluid therapy
b. dexamethasone (1 mg/kg IV)
c. intravenous administration of regular insulin followed by dextrose infusion
d. sodium bicarbonate
e. 10% calcium gluconate infusion over 10 to 15 minutes

8. For a patient with hypoadrenocorticism that is receiving maintenance DOCP therapy, therapeutic monitoring does not generally include
a. electrolyte evaluation 12 to 15 days after initial administration of DOCP.
b. an ACTH stimulation test 25 days after initial administration of DOCP.
c. electrolyte evaluation 25 days after initial administration of DOCP.
d. evaluation of clinical signs observed by the owner and alteration of the dose of prednisone as directed by the veterinarian.
e. electrolyte evaluation 25 days after the second administration of DOCP.

9. A dog with hypoadrenocorticism that was diagnosed 6 months ago presents with vomiting (which began recently at a boarding facility), diarrhea, and melena. The patient has been receiving monthly injections of DOCP and 0.1 mg/kg/day of prednisone. Which diagnostic and therapeutic measures should not be included in managing this patient?
a. Discontinue prednisone therapy; the dog may have an ulcer secondary to chronic steroid use and stress.
b. Measure the electrolyte level to ensure that the dose of DOCP does not need to be altered.
c. Administer 1 mg/kg of prednisone immediately; the dog was stressed and should have been given a supplement before boarding.
d. Conduct a fecal examination to ensure that the dog does not have a parasite.
e. Administer famotidine for symptomatic therapy.

10. What should owners be told about the prognosis of a dog diagnosed with hypoadrenocorticism?
a. Although the dog may initially respond to therapy, most dogs become resistant to treatment and die within 6 months.
b. Dogs are generally able to live for an extended period with the disease, but even appropriate therapy does not usually provide them with a good quality of life.
c. Patients respond well to maintenance therapy and rarely need follow-up care or their dose of medication altered after the first visit.
d. After the initial crisis, the prognosis is good, and dogs generally live a normal life if medication is given as directed and appropriate laboratory monitoring is provided as needed.
e. Dogs typically do poorly after the diagnosis, and most do not live through the initial crisis.