



An In-Depth Look:

CANINE
HYPOADRENOCORTICISM

Canine Hypoadrenocorticism: Pathogenesis and Clinical Features*

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ABSTRACT:

Hypoadrenocorticism (Addison's disease) is an uncommon disease in dogs. Young, female dogs are predisposed. The most common cause of primary hypoadrenocorticism has been proposed to be immune-mediated destruction of all three layers of the adrenal cortex. This results in mineralocorticoid (aldosterone) and glucocorticosteroid (cortisol) deficiency. Patients typically present with a history of waxing and waning or fulminant gastrointestinal (GI) signs or of acute collapse (i.e., hypoadrenocortical [addisonian] crisis). Physical examination may be normal; however, signs of hypovolemic shock are usually present in patients experiencing hypoadrenocortical crisis. Radiographic and ultrasonographic findings include nonspecific indications of hypovolemia and a thin left adrenal gland, respectively. The classic laboratory findings in hypoadrenocortical dogs are azotemia, hyperkalemia, and hyponatremia, with a sodium:potassium ratio of less than 27:1. Patients with "atypical" hypoadrenocorticism usually present with GI signs and do not have the classic laboratory abnormalities of typical hypoadrenocorticism.

*A companion article on diagnosis and treatment appears on page 121.

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Naturally occurring hypoadrenocorticism, commonly referred to as *Addison's disease*, was first reported in a dog in 1953.¹ It is an uncommon syndrome with an annual incidence of only 36 cases per 100,000 dogs.² Approximately 30% of these patients present with acute hypoadrenocorticism (i.e., hypoadrenocortical [addisonian] crisis).¹ Although hypoadrenocorticism is an uncommon disease, the typical clinical signs and laboratory abnormalities associated with it are commonly seen in patients that present to primary care and emergency clinics (Table 1). Therefore, hypoadrenocorticism is a common rule out for many patients seen in private or

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referral practice. Failure to recognize and diagnose hypoadrenocorticism in a timely manner can lead to prolonged, repeated, and costly administration of symptomatic therapy instead of definitive therapy as well as precipitation of an Addisonian crisis.

CAUSE

Hypoadrenocorticism is most commonly caused by primary adrenocortical failure involving all three layers of the adrenal cortex (i.e., zona glomerulosa, zona fasciculata, zona reticularis). Clinical signs develop because of decreased secretion of glucocorticosteroids (cortisol) from the zona fasciculata and zona reticularis as well as mineralocorticoids (aldosterone) from the zona glomerulosa.¹ Secondary hypoadrenocorticism caused by pituitary disease or cranial trauma has been rarely described in dogs.³ In a 1996 prospective study from The Animal Medical Center (AMC) in New York, only one of 42 dogs was afflicted with secondary hypoadrenocorticism.⁴ Secondary hypoadrenocorticism is characterized by decreased pituitary secretion of adrenocorticotrophic hormone (ACTH), resulting in atrophy of the zona fasciculata and zona reticularis and subsequent decrease in cortisol production and secretion. Because ACTH plays only a minor role in regulating aldosterone secretion from the zona glomerulosa, patients with secondary hypoadrenocorticism generally show clinical signs associated only with cortisol deficiency; they rarely have significant electrolyte abnormalities.^{1,4,5}

The most likely cause of primary hypoadrenocorticism in dogs is immune-mediated destruction of the adrenal

Table 1. Laboratory Abnormalities Associated with Hypoadrenocorticism¹

Abnormality	Dogs (%)
Hyperkalemia	92
Decreased sodium:potassium ratio	91
Increased blood urea nitrogen	90
Hyponatremia	84
Increased creatinine	61
Hypochloremia	46
Hypercalcemia	30
Normochromic, normocytic anemia	25
Hypoglycemia	20
Hypoalbuminemia	14 ³¹ –39 ³⁰
Absolute eosinophilia	14
Absolute lymphocytosis	13

Iatrogenic primary hypoadrenocorticism is caused by administering drugs that directly inhibit glucocorticoid production or adrenocortical lysis. Mitotane (o-p'-DDD; Lysodren, Bristol-Myers Squibb) is used to treat pituitary-dependent hyperadrenocorticism (i.e., Cushing's disease) because, if dosed using the standard published protocols, it causes dose-dependent progressive atrophy of the zona fasciculata and zona reticularis while sparing the zona glomerulosa.¹ However, patient monitoring is paramount because the duration of induction therapy and type of maintenance mitotane therapy

Addison's disease should be considered in all patients with hyperkalemia and hyponatremia.

cortex. However, the most commonly observed histopathologic lesion found in affected dogs is idiopathic atrophy of the adrenal cortex.^{1,6} Histologic evidence of inflammation may be absent because many dogs with Addison's disease undergo necropsy late in the disease process following long-term therapy. Uncommon causes of primary hypoadrenocorticism include infiltrative diseases (i.e., fungal infections and neoplasia), amyloidosis, hemorrhagic disorders, and coagulopathies, which result in bilateral adrenal gland destruction.¹

needed to achieve appropriate blood cortisol concentrations vary between patients. In addition, mitotane has been shown to cause nonselective destruction of the adrenal cortex, resulting in mineralocorticoid and glucocorticoid deficiency in 6% of patients treated with standard doses (i.e., a mean weekly dose of 53 mg/kg).⁷ This complication can occur even when published treatment protocols are followed; however, it is more likely at higher doses.⁸ The patient may present in adrenocortical crisis in either of these situations; thus

measuring electrolytes and response to an ACTH stimulation test should always be part of the diagnostic evaluation in sick Cushingoid patients that are being treated with mitotane.^{1,7,9}

An alternative protocol for treating pituitary-dependent hyperadrenocorticism involves administering high doses of mitotane (o-p'-DDD) to completely obliterate all layers of the adrenal cortex. During treatment and for the remainder of the dog's life, patients must be treated with mineralocorticoid and corticosteroid supplementation and are subject to the same long-term management regimens as are patients with naturally occurring primary hypoadrenocorticism.^{9,10} In addition, owners must be warned that these patients are at risk of a hypoadrenocortical crisis if medication is not given as directed.^{9,10} Prolonged administration of high doses of mitotane are also used to treat nonresectable or metastatic adrenocortical tumors. Patients with these tumors may also become glucocorticoid or mineralocorticoid deficient^{1,11} (Figure 1).

Trilostane, a competitive inhibitor of the enzyme 3β -hydroxysteroid dehydrogenase, decreases production of both corticosteroids and aldosterone. Reports on its use in treating canine hyperadrenocorticism have only recently been published.¹²⁻¹⁴ In a study of 78 hyperadrenocortical dogs treated with trilostane, two patients receiving high doses experienced hypoadrenocortical crises; both had hyperkalemia, hyponatremia, and inadequate responses to ACTH stimulation testing. One patient died despite supportive therapy and discontinuation of the drug. In addition, several other patients showed electrolyte disturbances consistent with Addison's disease but did not show clinical signs.¹³ This study suggests that, although trilostane appears to be an effective treatment of hyperadrenocorticism, proper monitoring (including electrolyte measurements and ACTH stimulation tests) is necessary to prevent hypoadrenocortical crises, particularly when high doses are used.

A subset of patients with primary hypoadrenocorticism does not have classic electrolyte abnormalities. In patients with normal electrolyte concentrations on repeated biochemical analyses and subnormal cortisol concentrations following ACTH stimulation testing, the diagnosis is atypical hypoadrenocorticism.¹⁵⁻¹⁸ Measuring endogenous ACTH levels helps confirm that the hypoadrenocorticism is due to primary adrenocortical failure and is not secondary to pituitary disease.^{16,18} Patients with atypical hypoadrenocorticism can be suc-

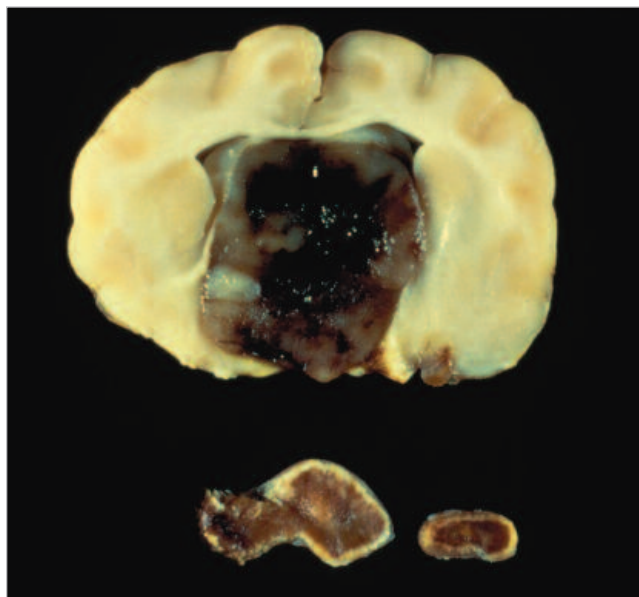


Figure 1. Brain and adrenal glands from a dog with a pituitary macroadenoma. The dog was treated with mitotane, resulting in adrenocortical atrophy and iatrogenic hypoadrenocorticism.

cessfully managed with corticosteroid therapy alone. However, most of these patients eventually develop electrolyte abnormalities within months or years of the initial diagnosis. This may suggest an ongoing destruction of the adrenal gland that begins with the zona fasciculata and zona reticularis and progresses to involve the zona glomerulosa.^{16,18}

Iatrogenic secondary hypoadrenocorticism results from prolonged corticosteroid administration through feedback inhibition of ACTH release from the anterior pituitary. The lack of ACTH results in atrophy of the zona fasciculata and zona reticularis of the adrenal cortex; the zona glomerulosa is not affected. The ability of the adrenal gland to respond to ACTH stimulation and produce cortisol is greatly diminished. Therefore, even though a dog being treated with glucocorticosteroids may show clinical signs associated with excess cortisol (i.e., Cushing's syndrome), it may actually have adrenocortical atrophy. When long-term daily or repository corticosteroid therapy is stopped, the animal is unable to respond adequately to ACTH and becomes cortisol deficient.¹⁹ A recent study demonstrated that 28 dogs that received long-term corticosteroid therapy (i.e., 1 to 36 months; mean: 9.4 months) had suppressed or absent adrenal responses to ACTH stimulation but did not show clinical signs of hypoadrenocorticism

following abrupt cessation of corticosteroid administration.²⁰ However, this study did not assess these dogs' ability to respond to a stressful situation. Inability to

white terrier.¹ Familial predispositions have been reported in the Portuguese water dog, Leonberger, Nova Scotia duck tolling retriever, standard poodle, and

Atypical addisonian patients do not have classic electrolyte abnormalities. An ACTH stimulation test should be part of the diagnostic plan in patients with chronic vomiting, diarrhea, or weight loss.

respond to a stressful event with appropriate adrenal production of glucocorticoids could precipitate a hypoadrenocortical crisis. Therefore, we still strongly recommend tapering the corticosteroid dose following long-term treatment.

SIGNALMENT

Addison's disease is most prevalent in young to middle-aged female dogs. Predisposed breeds include the Great Dane, poodle (all sizes), and West Highland

bearded collie; in the latter two breeds, the disease appears to affect both sexes equally.^{21–25}

PRESENTATION

Addison's disease often causes vague, nonspecific clinical signs that can be confused with a large number of different diseases, thus earning hypoadrenocorticism the moniker *the great pretender*.²⁶ The most common presenting complaints are anorexia, lethargy, vomiting, and weight loss.^{4,5,27–29} Most dogs have clinical signs consistent with primary or secondary gastrointestinal (GI) disease, including anorexia, vomiting, weight loss, diarrhea, and (less commonly) hematemesis, hematochezia, and/or melena. Polyuria/polydipsia and shaking/shivering have each been identified in about 17% of cases.¹ There is often a history of waxing and waning illness ameliorated by such nonspecific treatments as fluid therapy and corticosteroid administration.^{5,26} Muscle cramping was recently reported in two poodles diagnosed with hypoadrenocorticism; the cramping resolved with appropriate management.³⁰

Dogs that present in addisonian crisis often have the same histories and clinical signs as those that present with chronic hypoadrenocorticism. In our experience, they frequently have a history of waxing and waning disease that acutely exacerbates. Although they may have a history of chronic, intermittent GI signs, they might be presented because of an acute episode of vomiting and/or diarrhea with anorexia. They generally show signs of severe shock and hypovolemia. They may also have a history of recent collapse.⁵ In addition, severe GI hemorrhage, resulting in hematochezia and melena, has been reported in dogs that present in addisonian crisis.³¹ Correct diagnosis can be challenging because electrolyte abnormalities (i.e., hyperkalemia) may not be present or may initially be attributed to loss from the GI tract (i.e., hyponatremia). Hyperkalemia

and hyponatremia may develop after initial treatment of patients with acute disease.⁵

Physical examination commonly reveals depression, weakness, and dehydration.^{4,5,27,28} Bradycardia is present in only approximately 22% of cases; however, the presence of bradycardia or an inappropriately normal heart rate in the presence of hypovolemia should prompt clinicians to suspect hypoadrenocorticism because hyperkalemia inhibits the normal physiologic response of tachycardia.^{1,32}

Atypical Addisonian patients generally present with nonspecific clinical signs, including lethargy, weight loss, and GI disease (i.e., vomiting, diarrhea, anorexia).^{15,16,18,33} They may also present in acute collapse despite normal electrolyte values.¹⁸ Hypoglycemic seizures have also been reported in patients with atypical hypoadrenocorticism.^{18,33}

RADIOGRAPHIC AND ULTRASONOGRAPHIC ABNORMALITIES

Abdominal and thoracic radiography are frequently part of the diagnostic workup for dogs that present in acute collapse or shock; abdominal radiography and ultrasonography are indicated in patients that present with problems referable to the abdominal cavity and GI tract. Thus thoracic and abdominal radiography are frequently used in

ing the relationship of the liver to the stomach, kidneys, and other abdominal organs. Results indicated that 18 of the 22 dogs had one or more of the following radiographic abnormalities: microcardia, small cranial lobar pulmonary artery or caudal vena cava, and microhepatica. Each of these abnormalities was found in one-third to one-half of the dogs. These abnormalities could be attributed to any disease resulting in hypovolemia and are not pathognomonic for hypoadrenocorticism. Instead, they suggest that hypoadrenocorticism should be ruled out in dogs that present with nonspecific clinical signs and these radiographic abnormalities. In addition to these findings, the study found no evidence of megaesophagus in any of the dogs.³⁴ However, reversible megaesophagus has been reported in both typical and atypical Addisonian patients; thus although hypoadrenocorticism is a rare cause, it should remain a diagnostic differential in determining the cause of megaesophagus.^{18,36,37}

In a study published in 1999,³⁸ ultrasonography revealed decreased left adrenal gland length and thickness in untreated patients with hypoadrenocorticism (the right adrenal gland was not visualized in enough subjects to include the results). In five of six subjects, adrenal gland thickness was found to be less than that in the normal dogs. The authors concluded that, although there is some

An ECG should be obtained for all patients that present in hypovolemic shock. The ECG may be the first indication that a patient is hyperkalemic.

patients that are eventually diagnosed with hypoadrenocorticism. Although radiography does not usually contribute to the diagnosis of Addison's disease, it can help clinicians rule out other diseases that cause similar clinical signs.

A 1999 AMC study described some nonspecific radiographic abnormalities that are commonly present in patients with hypoadrenocorticism.³⁴ Radiographic parameters of 22 untreated dogs with primary hypoadrenocorticism were measured using standardized, objective guidelines. The vertebral scale system was used to measure heart size,³⁵ the pulmonary artery:fourth rib ratio was used to compare the size of the cranial lobar pulmonary artery with the width of the fourth rib, and the vena cava:length of T5 ratio was used to compare the width of the caudal vena cava with the length of the fifth thoracic vertebra. Liver size was measured by determin-

overlap between normal and hypoadrenocortical patients, ultrasonography might be a useful screening tool in patients suspected of having hypoadrenocorticism.³⁸

ELECTROCARDIOGRAPHIC ABNORMALITIES

An electrocardiographic evaluation is indicated in all patients that present with signs of shock and/or a history of acute collapse. Abnormalities on an electrocardiogram (ECG) may be the first indication of hyperkalemia in some patients. Because of the life-threatening effects of hyperkalemia, diagnosis by ECG may prompt life-saving treatment regardless of the primary cause of hyperkalemia. Increased T wave amplitude (i.e., positive or negative deflection) and bradycardia begin to appear with mild hyperkalemia (i.e., 5.6 to 6.5 mEq/L). These

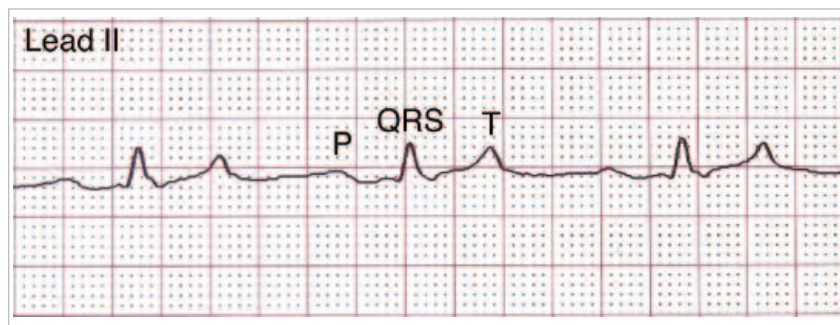


Figure 2. Lead II ECG (50 mm/sec; 1 cm = 1 mV) from an Addisonian patient with a serum K^+ concentration of 8 mEq/L at presentation. The QRS complex is widened, the R wave amplitude is decreased, and the P wave is flattened. The dog was severely hypovolemic, and its heart rate was only 120 bpm.

changes may diminish or resolve as the potassium concentration increases, intraventricular conduction disturbances mask the T wave changes, and hypoxia increases the heart rate.¹ The QRS complex begins to widen and the R wave amplitude decreases as hyperkalemia becomes more severe. The P wave flattens and first-degree heart block commonly develops as the potassium concentration increases further. Marked hyperkalemia commonly causes atrial standstill and loss of visible P waves. This results in a sinoventricular rhythm. As serum potassium levels continue to increase, the QRS complexes become progressively wider and more unusual. These ECG abnormalities resemble those seen in patients with ventricular tachycardia or supraventricular tachycardia with a bundle-branch block. However, both of these arrhythmias are characterized by tachycardia, a regular rhythm, and the presence of P waves that may not be related to the QRS complex. P waves are not present in patients with a sinoventricular rhythm, and the heart rate is usually bradycardic or normal. The rhythm may be regular or irregular. Terminally, as hyperkalemia escalates, ventricular flutter, fibrillation, or asystole develops. The absence of these ECG findings does not preclude the possibility that hyperkalemia exists because classic abnormalities may not occur in a given hyperkalemic patient^{1,27,32,39} (Figure 2).

LABORATORY ABNORMALITIES: PREVALENCE AND PATHOPHYSIOLOGY

The classic laboratory abnormalities in dogs with hypoadrenocorticism are hyponatremia and hyperkalemia.^{1,2,4,5,28,29,34} Almost all the dogs in the 1996 prospective AMC study were also hyperphosphatemic

and had prerenal azotemia.⁴ Of dogs that presented with hypoadrenocorticism, 92% and 84% have reportedly had hyperkalemia and hyponatremia, respectively.¹ The presence of hypoaldosteronism explains many of the electrolyte abnormalities associated with primary hypoadrenocorticism. The major role of aldosterone is to promote sodium and water absorption as well as potassium excretion through an exchange process in the distal renal tubule. To a lesser extent, aldosterone also causes tubular excretion of hydrogen ions in exchange for sodium.^{40,41} Thus aldosterone deficiency results not only in impaired sodium and

water resorption but also in decreased potassium and acid excretion. Consequently, hypovolemia, hyponatremia, hyperkalemia, and metabolic acidosis may all result. Hypovolemia further exacerbates the electrolyte disturbances by stimulating antidiuretic hormone release from the hypothalamus. Antidiuretic hormone increases free water retention from the medullary collecting ducts, thus diluting the already deficient plasma sodium concentration.^{1,26,40}

Hypercalcemia occurs in approximately 30% of all untreated hypoadrenocortical dogs, although it is much more common in severe cases. The precise cause of hypercalcemia in Addisonian patients is unknown, but several theories have been proposed. In normal dogs, corticosteroids promote calciuresis. The excessive renal tubular reabsorption of calcium in adrenalectomized dogs suggests that decreased calciuresis is an important factor in the hypercalcemia seen in Addisonian dogs. Hyperproteinemia secondary to hemoconcentration may also contribute to the hypercalcemia seen in some Addisonian patients. By inhibiting vitamin D, glucocorticoids decrease intestinal absorption of calcium; therefore, hypocortisolemia could lead to increased intestinal absorption of calcium and hypercalcemia. However, this mechanism does not appear to be a significant cause of hypercalcemia in dogs with hypoadrenocorticism.⁴² Regardless of the cause, hypercalcemia in Addisonian patients rarely causes clinical signs, resolves following volume expansion, and remains normal with appropriate hormone replacement therapy.^{1,2,42}

Azotemia is a very common finding in dogs with hypoadrenocorticism and is usually prerenal in nature. It is caused by decreases in renal perfusion and the

glomerular filtration rate that develop secondary to the hypovolemia and hypotension typically present in patients with hypoadrenocorticism.^{4,5,28,29} In some dogs, prerenal azotemia can be attributed to or exacerbated by GI hemorrhage. Although the presence of adequate urine concentrating ability (as evidenced by a urine specific gravity >1.030) is usually sufficient to differentiate between prerenal and renal azotemia,⁴³ 88% of dogs with hypoadrenocorticism have reportedly had urine specific gravities lower than 1.030.¹ This lack of appropriate urine concentration may be the result of decreased renal medullary tonicity caused by sodium depletion⁴⁴ or tubular dysfunction or renal failure caused by renal hypoxia.^{1,5} Because of severe azotemia and inadequate urine-concentrating ability, patients with hypoadrenocorticism are often initially misdiagnosed with acute renal failure. Because of the difference in treatment and prognosis, it is imperative that the dis-

ever, has reportedly been between 3%²⁷ and 37.5%.^{1,4,5,28} Furthermore, although 14 of 42 (33.3%) dogs in a 1996 AMC study were hypoglycemic, only three (7%) dogs had symptomatic neuroglycopenia characterized by extreme weakness and seizures.⁴ Hypoglycemia has also been reported in atypical Addisonian patients; thus although hypoglycemia may not be that common in hypoadrenal dogs, hypoadrenocorticism should be a differential in patients with symptomatic or asymptomatic hypoglycemia.^{12,15,16,18,19,47}

Abnormalities also exist in hemograms of untreated dogs with hypoadrenocorticism. Partly because steroids play a role in stimulating erythropoiesis in bone marrow, anemia has been reported in 14%²⁷ to 43%²⁸ of dogs with hypoadrenocorticism,^{1,4,29} with an incidence of 26.7% in the largest study (225 dogs).⁵ Dogs with the most severe anemia (packed cell volume: <20%) are more likely to also have GI blood loss.⁵ The most com-

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tion is made. In most animals with prerenal azotemia (such as those with hypoadrenocorticism), blood urea nitrogen levels begin to return to normal within 12 hours after initiating treatment and should be normal within 1 to 3 days. Renal azotemia responds much more slowly, if at all, to fluid therapy, and normalization of renal parameters rarely occurs. In patients with hypoadrenocorticism, azotemia that does not improve within 24 hours of initiating appropriate fluid therapy may be attributed to either renal damage secondary to hypoperfusion or concurrent renal failure.⁴⁵

Hypoalbuminemia has reportedly been present in up to 40% of dogs diagnosed with hypoadrenocorticism. It may result from GI blood loss. Other possible mechanisms include protein-losing enteropathy, malassimilation, and decreased albumin synthesis.^{5,46}

Because glucocorticosteroids stimulate hepatic gluconeogenesis and promote formation of hepatic glycogen, the decreased cortisol concentrations in dogs with hypoadrenocorticism should intuitively cause fasting hypoglycemia.^{1,34} The incidence of hypoglycemia, how-

ever, has reportedly been between 3%²⁷ and 37.5%.^{1,4,5,28} Furthermore, although 14 of 42 (33.3%) dogs in a 1996 AMC study were hypoglycemic, only three (7%) dogs had symptomatic neuroglycopenia characterized by extreme weakness and seizures.⁴ Hypoglycemia has also been reported in atypical Addisonian patients; thus although hypoglycemia may not be that common in hypoadrenal dogs, hypoadrenocorticism should be a differential in patients with symptomatic or asymptomatic hypoglycemia.^{12,15,16,18,19,47}

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CONCLUSION

Hypoadrenocorticism is an uncommon disease that should be considered in the diagnostic evaluation of all patients that present with GI signs and/or acute collapse. Although classic laboratory abnormalities (including hyponatremia and hyperkalemia) exist in most patients with Addison's disease, lack of these abnormalities does not rule out hypoadrenocorticism. Hypoad-

renocorticism should also be considered in patients with various nonclassic laboratory abnormalities, including lack of a stress leukogram despite moderate to severe illness. An ACTH stimulation test should be conducted in patients suspected of having the disease, and proper treatment should be provided when applicable.

REFERENCES

- Feldman EC, Nelson RW: *Canine and Feline Endocrinology and Reproduction*, ed 3. Philadelphia, WB Saunders, 2003, pp 394–435.
- Reusch CE: Hypoadrenocorticism, in Ettinger SJ, Feldman EC (eds): *Textbook of Veterinary Internal Medicine*, ed 5. Philadelphia, WB Saunders, 2000, p 1488.
- Platt SR, Chrisman CL, Graham J, Clemmons RM: Secondary hypoadrenocorticism associated with craniocerebral trauma in a dog. *JAAHA* 35:117–122, 1999.
- Melian C, Peterson ME: Diagnosis and treatment of naturally occurring hypoadrenocorticism in 42 dogs. *J Small Anim Pract* 37:268–275, 1996.
- Peterson ME, Kintzer PP, Kass PH: Pretreatment clinical and laboratory findings in dogs with hypoadrenocorticism: 225 cases (1979–1993). *JAVMA* 208:85–91, 1996.
- Schaer M, Riley WJ, Buergelt CD, et al: Autoimmunity and Addison's disease in the dog. *JAAHA* 22:789–794, 1986.
- Kintzer PP, Peterson ME: Mitotane (o,p'-DDD) treatment of 200 dogs with pituitary-dependent hyperadrenocorticism. *J Vet Intern Med* 5:182–190, 1991.
- Willard MD, Schall WD, Nachreiner RF, et al: Hypoadrenocorticism following therapy with o,p'-DDD for hyperadrenocorticism in four dogs. *JAVMA* 180:638–641, 1982.
- Hertog ED, Breakman JC, Teske E, et al: Results of non-selective adrenocorticolysis by o,p'-DDD in 129 dogs with pituitary-dependent hyperadrenocorticism. *Vet Rec* 144:12–17, 1999.
- Rijnberk A, Belshaw BE: An alternative protocol for the medical management of canine pituitary-dependent hyperadrenocorticism. *Vet Rec* 122:486–488, 1988.
- Kintzer PP, Peterson ME: Mitotane (o,p'-DDD) treatment of hyperadrenocorticism in dogs, in Bonagura JD, Kirk RW (eds): *Current Veterinary Therapy XII: Small Animal Practice*. Philadelphia, WB Saunders, 1995, pp 416–420.
- Ruckstuhl NS, Nett CS, Reusch CE: Results of clinical examinations, laboratory tests, and ultrasonography in dogs with pituitary-dependent hyperadrenocorticism treated with trilostane. *AVJR* 63:506–512, 2002.
- Neiger R, Ramsey I, O'Connor J, et al: Trilostane treatment of 78 dogs with pituitary-dependent hyperadrenocorticism. *Vet Rec* 150:799–804, 2002.
- Hurely K, Sturgess K, Cauvia A, et al: The use of trilostane for the treatment of hyperadrenocorticism in dogs (abstr). *Proc 16th Am Coll Vet Intern Med Forum*:700, 1998.
- Sadek D, Schaer M: Atypical Addison's disease in the dog: A retrospective survey of 14 cases. *JAAHA* 32:159–163, 1996.
- Rogers W, Straus J, Chew D: Atypical hypoadrenocorticism in three dogs. *JAVMA* 179:155–158, 1981.
- Bruyette D, Behrend E, Scott-Moncrieff C, et al: *Addison's Disease: Uncommon or Underdiagnosed?* Lenexa, KS, Novartis Animal Health, 2003.
- Lifton SJ, King LG, Zerbe CA: Glucocorticoid deficient hypoadrenocorticism in dogs: 18 cases (1986–1995). *JAVMA* 209:2076–2081, 1996.
- Romatowski J: Iatrogenic adrenocortical insufficiency in dogs. *JAVMA* 196:1144–1146, 1990.
- Huang H, Yang H, Liang S, et al: Iatrogenic hyperadrenocorticism in 28 dogs. *JAAHA* 25:200–207, 1999.
- Shaker E, Hurvitz A, Peterson M: Hypoadrenocorticism in a family of standard poodles. *JAVMA* 192:1091–1092, 1988.
- Famula TR, Belanger JM, Oberbauer AM: Heritability and complex segregation analysis of hypoadrenocorticism in the standard poodle. *J Small Anim Pract* 44:8–12, 2003.
- Oberbauer AM, Benemann KS, Belanger JM, et al: Inheritance of hypoadrenocorticism in bearded collies. *Am J Vet Res* 63:643–647, 2002.
- Smallwood LJ, Barsanti JA: Hypoadrenocorticism in a family of Leonbergers. *JAAHA* 31:301–305, 1995.
- Burton S, DeLay J, Holmes A, et al: Hypoadrenocorticism in young related Nova Scotia duck tolling retrievers. *Can Vet J* 38:231–234, 1997.
- Podell M: Canine hypoadrenocorticism: Diagnostic dilemmas associated with the "great pretender." *Probl Vet Med* 2(4):717–737, 1990.
- Willard MD, Schall WD, McCaw DE: Canine hypoadrenocorticism: Report of 37 cases and review of 39 previously reported cases. *JAVMA* 180:59–62.
- Rakich PM, Lorenz MD: Clinical signs and laboratory abnormalities in 23 dogs with spontaneous hypoadrenocorticism. *JAAHA* 20:647–649, 1984.
- Schaer M, Chen CL: A clinical survey of 48 dogs with adrenocortical hypofunction. *JAAHA* 19:443–452, 1983.
- Saito M, Olby NJ, Obledo L, Gookin JL: Muscle cramps in two standard poodles with hypoadrenocorticism. *JAAHA* 38:437–443, 2002.
- Medinger TL, Williams DA, Bruyette DS: Severe gastrointestinal tract hemorrhage in three dogs with hypoadrenocorticism. *JAVMA* 202:1869–1872, 1993.
- Schaer M: The treatment of acute adrenocortical insufficiency in the dog. *J Vet Emerg Crit Care* 11:7–14, 2001.
- Levy JK: Hypoglycemic seizures attributable to hypoadrenocorticism in a dog. *JAVMA* 204:526–529, 1994.
- Melian C, Stefanic J, Peterson ME, Kintzer PP: Radiographic findings in dogs with naturally occurring primary hypoadrenocorticism. *JAAHA* 35:208–212, 1999.
- Buchanan JW, Bucheler J: Vertebral scale system to measure canine heart size in radiographs. *JAVMA* 206:194–199, 1995.
- Bartges JW, Nielson DL: Reversible megaesophagus associated with atypical primary hypoadrenocorticism in a dog. *JAVMA* 201:889–891, 1992.
- Whitley NT: Megaesophagus and glucocorticoid-deficient hypoadrenocorticism in a dog. *J Small Anim Pract* 36:132–135, 1995.
- Hoerauf A, Reusch C: Ultrasonographic evaluation of the adrenal glands in six dogs with hypoadrenocorticism. *JAAHA* 35:214–218, 1999.
- Feldman EC, Ettinger SJ: Electrocardiographic changes associated with electrolyte disturbances. *Vet Clin North Am Small Anim Pract* 7:487–496, 1977.
- Guyton AC, Hall JE: *Textbook of Medical Physiology*, ed 9. Philadelphia, WB Saunders, 1996.
- 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.
- Peterson ME, Feinman JM: Hypercalcemia associated with hypoadrenocorticism in 16 dogs. *JAVMA* 181:802, 1982.
- Cowgill LD, Elliott DA: Acute renal failure, in Ettinger SJ, Feldman EC (eds): *Textbook of Veterinary Internal Medicine*, ed 5. Philadelphia, WB Saunders, 2000, pp 1615–1633.
- Tyler RD, Qualls CW, Heald D, et al: Renal concentrating ability in dehydrated hyponatremic dogs. *JAVMA* 9:1095–1100, 1987.
- Osborne CA, Polzin DJ: Azotemia: A review of what's old and what's new. Part II: Localization. *Compend Contin Educ Pract Vet* 5:561–574, 1983.
- Langlais-Burgess L, Lumsden JH, Mackin A: Concurrent hypoadrenocorticism and hypoalbuminemia in dogs: A retrospective study. *JAAHA* 31:307–311, 1995.
- Syme HM, Scott-Moncrieff JC: Chronic hypoglycaemia in a hunting dog due to secondary hypoadrenocorticism. *J Small Anim Pract* 39:348–351, 1998.

ARTICLE #2 CE TEST

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- 1. What is the most likely cause of most cases of canine hypoadrenocorticism?**
 - a. viral infection
 - b. bacterial infection
 - c. neoplasia
 - d. immune-mediated disease
 - e. trauma
- 2. Which disease has not been reported to cause primary hypoadrenocorticism?**
 - a. immune-mediated disease
 - b. fungal infection
 - c. neoplasia
 - d. coagulopathy
 - e. prolonged steroid administration
- 3. Which of the following is not a proposed mechanism for hypercalcemia exhibited by Addisonian dogs?**
 - a. decreased calciuresis
 - b. excessive renal tubular resorption of calcium
 - c. hyperproteinemia
 - d. increased activity of vitamin D in the small intestine
 - e. increased levels of parathyroid-related protein
- 4. Which of the following is not a likely contributing factor to azotemia in patients with hypoadrenocorticism?**
 - a. increased blood ammonia secondary to liver failure
 - b. severe hypovolemia
 - c. GI hemorrhage
 - d. renal damage secondary to hypoperfusion
 - e. dehydration
- 5. Which layer(s) of the adrenal cortex is affected in most patients with primary hypoadrenocorticism?**
 - a. zona glomerulosa
 - b. zona reticularis
 - c. zona fasciculata
 - d. a, b, and c
 - e. none of the above—primary disease affects the pituitary
- 6. Which statement regarding aldosterone is incorrect?**
 - a. Aldosterone is secreted by the zona glomerulosa of the adrenal cortex.
 - b. Aldosterone promotes sodium resorption in the distal convoluted tubules.
 - c. Aldosterone promotes chloride excretion in the distal convoluted tubules.
 - d. Aldosterone promotes potassium excretion in the distal convoluted tubules.
 - e. Aldosterone promotes hydrogen ion excretion in the distal convoluted tubule.
- 7. Which ECG finding has not been commonly reported in patients with hyperkalemia?**
 - a. increased T wave amplitude
 - b. widened QRS complexes
 - c. flattened P waves
 - d. asystole
 - e. sinus tachycardia
- 8. Which physical examination finding is not common in patients with hypoadrenocorticism?**
 - a. dyspnea
 - b. dehydration
 - c. bradycardia
 - d. depression
 - e. melena
- 9. Which finding has not been reported in patients with hypoadrenocorticism?**
 - a. microhepatica on radiographs
 - b. increased left adrenal gland thickness on an ultrasound
 - c. reversible megaesophagus
 - d. microcardia on radiographs
 - e. small cranial lobar pulmonary artery on radiographs
- 10. Which clinical sign is not commonly reported in patients with hypoadrenocorticism?**
 - a. vomiting
 - b. polyphagia
 - c. polyuria
 - d. melena
 - e. muscle cramping