Managing Canine Addisonian Crisis

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Hypoadrenocorticism, or Addison's disease, is an endocrine disorder characterized by insufficient production of glucocorticoids (eg, cortisol) and/or mineralocorticoids (eg, aldosterone).[1-3] Cortisol is necessary for gluconeogenesis, stress adaptation, immune function, gastrointestinal mucosal integrity, and catecholamine-mediated vasoconstriction,[1-3] while aldosterone maintains normal blood volume and blood potassium concentration.[1-3]

See client handout, **Addison's Disease**, at brief.vet/canine-addisonian-crisis

A patient in Addisonian crisis is in shock—a state of inadequate cellular energy production that causes death if left untreated.[4] Shock results from sequelae of hypoadrenocorticism, primarily hypovolemia. Other contributing factors are paradoxical bradycardia, vasodilation, hypoglycemia, and, in some cases, severe anemia from blood loss via the gastrointestinal tract.[2,3] Hypoadrenocorticism is not common, but in those affected, up to one-third will be presented in Addisonian crisis.[5] (See **Resources**, page 30.)

The typical patient with Addison's disease is a young to middle-aged spayed female dog; the disease also occurs in puppies, geriatric dogs, neutered male dogs, and intact dogs of both sexes.[3,6] Although certain breeds are at increased risk for Addison's disease (see **Pure-Breed Dogs at Increased Risk for Hypoadrenocorticism**), any breed can be affected,[3,6,7] and studies have shown mixed-breed dogs are diagnosed more often than any individual breed.[6,7]

Clinical signs include lethargy, waxing and waning gastrointestinal signs, weight loss, thin body condition, polyuria and polydipsia, and numerous other nonspecific signs. Any event that causes fear or anxiety may worsen clinical signs because cortisol regulates the body's reaction to stress. A peracute presentation with no apparent history is also possible, and an Addisonian crisis can occur in a patient already diagnosed with and being treated for hypoadrenocorticism. (See **Resources**, page 30.)

Fluid resuscitation is the single most important therapy, as it restores circulating blood volume and helps correct severe electrolyte abnormalities.

Diagnosis

Diagnosis requires recognition of both shock and underlying hypoadrenocorticism based on the patient's history, physical examination findings, and initial clinicopathologic data. Most patients in shock exhibit signs of abnormal perfusion, including[2,4,8]:

- Dull mentation
- Pale gums
- Delayed capillary refill time (>2 seconds)
- Poor pulses
- Paradoxical bradycardia
- Hypothermia

Some patients appear falsely alert and stable during the early stages of shock when physiologic compensation occurs.[4]

Diagnostic tests for shock include a minimum database consisting of a CBC, serum chemistry profile, and urinalysis. Measurement of blood lactate concentration (normal, <2.5 mmol/L) can also be used to confirm shock, quantify its severity, and monitor the patient's response to fluid resuscitation therapy.[4,9,10]

Common characteristics of patients experiencing an Addisonian crisis are listed in **Common Abnormalities in Dogs with Hypoadrenocorticism**.[6] A recent study[11] found evaluating the sodium:potassium ratio with the lymphocyte count was more effective to screen for hypoadrenocorticism than reviewing the sodium:potassium ratio alone. For example, presence of a low sodium:potassium ratio and absence of a stress leukogram is highly suggestive of hypoadrenocorticism. These clinicopathologic abnormalities, combined with signalment, history, and clinical signs of shock, increase likelihood of an Addisonian crisis.

If complete blood study results cannot be obtained quickly, blood glucose, blood urea nitrogen, packed cell volume, total solids, and electrolyte values can be used to guide initial treatment decisions. Alternatively, a venous blood gas also provides basic information as well as the patient's acid-base status.

A hypoadrenocorticism diagnosis cannot be confirmed by results of routine blood tests alone, however, because multiple clinicopathologic abnormalities may be associated with this disorder, earning the condition the colloquial nickname "The Great Pretender." **Diseases That Mimic Hypoadrenocorticism** lists several diseases or conditions that an Addisonian crisis can mimic.

Noninvasive blood pressure measurement to detect hypotension and monitor response to fluid resuscitation therapy also aids in evaluating patients with suspected hypoadrenocorticism.[2,4,8] Shock can be present when blood pressure is normal.[4] An ECG can disclose cardiac dysfunction secondary to hyperkalemia, as evidenced by tall, spiked T-waves, widened QRS complexes, absent P-waves, or atrial standstill. Normal ECG does not rule out hyperkalemia.[12]

A definitive diagnosis of Addison's disease requires an adrenocorticotropic hormone (ACTH) stimulation test and should be performed if the index of suspicion is high.[1,3] This test is performed by obtaining paired serum samples that measure cortisol concentrations before and 1 hour following administration of a 5 µg/kg dose of cosyntropin.[13] A single resting cortisol level (normal, >2 µg/dL) is a less expensive means of ruling out Addison's disease and serves as a reasonable screening test.[14] However, a low abnormal result (<2 µg/dL) does not confirm the diagnosis.

Pure-Breed Dogs at Increased Risk for Hypoadrenocorticism[2,3,6]

- Airedale terrier
- Basset hound
- Bearded collie
- Great Dane
- Leonberger
- Nova Scotia duck tolling retriever
- Pomeranian
- Portuguese water dog
- Rottweiler
- Saint Bernard
- Springer spaniel
- Standard poodle
- West Highland white terrier
- Wheaten terrier

Common Abnormalities in Dogs with Hypoadrenocorticism[1-3]

- Absence of stress leukogram (normal-to-high lymphocyte count)
- Azotemia
- Decreased sodium: potassium ratio
- Dilute urine specific gravity
- Hyperkalemia
- Hypoglycemia
- Hyponatremia
- Hypoproteinemia
- Metabolic acidosis
- Nonregenerative anemia

Diseases that Mimic Hypoadrenocorticism[1-3]

- Acute renal failure
- Gastroenteritis
- Hepatic failure
- Insulinoma
- Portosystemic shunt
- Protein-losing enteropathy
- Sepsis/septic shock
- Severe gastric ulceration with blood loss
- Xylitol toxicity

Treatment

Fluid Therapy

Successful management of an Addisonian crisis requires the aggressive correction of shock, electrolyte abnormalities, and other life-threatening sequelae, while concurrently pursuing a definitive diagnosis.

Appropriate treatment begins immediately after the initial triage examination has confirmed the presence of shock. Fluid resuscitation is the single most important therapy, as it restores circulating blood volume and helps correct severe electrolyte abnormalities.[2,8,15] A balanced crystalloid (eg, lactated Ringer's, Plasma-Lyte, or Normosol-R) is the fluid of choice for stabilization.[2,8,15] Physiologic saline (0.9% NaCl) is less ideal because it slows correction of concurrent metabolic acidosis and can correct hyponatremia too rapidly.[2,3,15-17]

Fluids should be administered as titrated boluses of 20 to 30 mL/kg intravenously (IV) over 10 to 20 minutes to effect.[2,15] Outcomes in patients with shock have improved when fluid resuscitation is continued until blood lactate concentration is normalized within the first 6 hours after a patient is presented to the practice.[9,10]

Hyperkalemia & Hypoglycemia

As serum chemistry values become known during the initial stabilization period, life-threatening abnormalities (eg, hyperkalemia, hypoglycemia) should be treated. If hyperkalemia is present, follow the adage "treat the patient, not the number." Addisonian crisis patients typically tolerate higher potassium concentrations (up to 7 to 8 mEq/L), and levels can stabilize with fluid therapy alone.[2,15] If the physical examination or an ECG suggests cardiac dysfunction, calcium gluconate may be administered IV as a short-acting cardioprotectant for approximately 10 to 20 minutes.[2,15]

Ideally, a continuous ECG should be obtained during calcium gluconate administration. A dextrose bolus IV also aids in hyperkalemia treatment, as the resultant endogenous insulin release lowers potassium concentrations via intracellular translocation. Insulin should be used judiciously (if at all), because abnormal gluconeogenesis prevents appropriate compensation if hypoglycemia occurs.[2,15]

Alternatively, β-adrenergic agonists (eg, albuterol, terbutaline) may offer a similar potassium-lowering effect without the danger of hypoglycemia.[15,18] **Table 1** summarizes these treatments.

Hypoglycemia can be treated with a dextrose bolus IV given to effect.[2,15] If necessary, dextrose may be added to the IV fluid therapy bag at a concentration of 2.5 percent or 5 percent to maintain normoglycemia.

TABLE **1** | **Common Treatments for Hyperkalemia**[2,15]

Name	Comments
Balanced crystalloid	Administer IV as a bolus over 10 to 20 minutes
Dextrose 50%	Dilute the total volume 1:4 with sterile water Administer IV slowly over 10 minutes
Calcium gluconate 10%	Administer IV slowly over 10 to 20 minutes
Albuterol	Inhaled
Terbutaline	Administer subcutaneously or IM only
Insulin (regular)	Administer IV Use with caution in cases refractory to fluids and other therapies Monitor for hypoglycemia

Poststabilization Supportive Therapy

Correction of hypovolemic shock, hyperkalemia, and hypoglycemia are key to successful management of an Addisonian crisis. After the patient has been stabilized with fluid resuscitation, fluid therapy may be continued to replace deficits related to dehydration and ongoing losses, meet maintenance fluid requirements, and correct electrolyte abnormalities. (Calculating a daily fluid therapy plan is well reviewed elsewhere.[19])

As a general rule, most patients require at least 2 to 3 times their daily maintenance fluid requirement during the first 24 to 48 hours of hospitalized care. For patients with severe hyponatremia (<120 mEq/L), sodium should be corrected slowly and raised no more than 10 mEq/L the first 24 hours and 18 mEq/L the first 48 hours.[20] Rapid correction of sodium concentration has been reported to cause severe neurologic signs secondary to myelinolysis of the central nervous system.[20,21]

In addition to continued fluid therapy, antiemetics and gastroprotectants are indicated for most patients. Analgesics and antibiotics may be administered as clinically indicated. Nonsteroidal anti-inflammatory drugs are contraindicated because of the eventual need for glucocorticoid therapy. Uncommonly, blood products (eg, whole blood, packed red blood cells) can be required to correct severe blood loss anemia secondary to gastric ulceration. Other supportive therapies should be provided based on the patient's clinical signs and needs.

Steroid Hormone Replacement Therapy

ACTH testing must be completed before rapidly acting glucocorticoids (eg, hydrocortisone sodium succinate, prednisone) can be administered. (Hydrocortisone sodium succinate also has mild mineralocorticoid activity.[8]) Dexamethasone does not interfere with cortisol assays and can be administered prior to ACTH testing if clinically indicated[3]; it can be given until oral prednisone is initiated.[3]

Oral prednisone may be used for long-term management at standard physiologic dosages once patients are eating and drinking regularly.[3] It may also be used during hospitalization at higher dosages if the patient can tolerate oral medications. Paradoxically, steroids are still indicated if gastric ulceration is present during an Addisonian crisis because cortisol is necessary for gastrointestinal mucosal integrity.

Key Client Communication Points

- Addison's disease (also called hypoadrenocorticism) is caused by an insufficiency of 2 hormones in the body (ie, cortisol, aldosterone) that are essential for maintaining normal body functions.
- An Addisonian crisis is a life-threatening emergency that occurs when a patient with Addison's disease develops shock from severe dehydration and electrolyte abnormalities.
- An Addisonian crisis diagnosis requires blood tests to determine how the crisis has affected the patient and to confirm the diagnosis of Addison's disease.
- All patients in Addisonian crisis require hospitalization for treatment and monitoring. Treatment consists of IV fluids to correct dehydration and electrolyte abnormalities, and other medications to control clinical signs. The hospital stay can range between 1 and 3 days, or longer, depending on the severity of the crisis.
- Even though an Addisonian crisis is severe and potentially life-threatening, the prognosis for a complete recovery is good.
- Lifelong therapy is required after the initial Addisonian crisis has been treated. Many patients receive a once-monthly injection (eg, DOCP) to maintain electrolyte balance and a once-daily pill (eg, prednisone) to control other signs. Periodic progress examinations are needed to monitor response to therapy.

Mineralocorticoid therapy is not needed to successfully manage an Addisonian crisis and may be contraindicated if severe hyponatremia is present, because mineralocorticoids can rapidly correct sodium concentrations, leading to complications.[2] Mineralocorticoids typically are administered at standard dosages once the patient is stable, eating, and drinking, and the results of ACTH testing confirm hypoadrenocorticism. Long-acting mineralocorticoids (eg, deoxycorticosterone pivalate [DOCP]) have largely replaced short-acting formulations such as fludrocortisone acetate.

Conclusion

Despite the potential for life-threatening sequelae, the prognosis for patients in Addisonian crisis is good with timely recognition and appropriate treatment. Aggressive fluid therapy and normalization of electrolyte abnormalities are the cornerstones of therapy, and corticosteroids are a necessary part of the initial treatment plan. Mineralocorticoid therapy should not be started until the patient is stable, appropriately diagnosed, and ready for discharge.

Patients with hypoadrenocorticism can live relatively normal lives; however, appropriate communication with the client (see **Key Client Communication Points**, page 29) regarding long-term management of Addison's disease is crucial to ensure patient quality of life and client satisfaction with patient care. ▬

References

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Resources

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- **Canine hypoadrenocorticism: pathogenesis, diagnosis, and treatment**. Van Lanen K, Sande A. *Topics in Compan An Med*. 2014;29:88-95.
- **Endocrine emergencies in dogs and cats**. Koenig A. *Vet Clin Small Anim*. 2013;43:869-897.

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