Potassium Disorders

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Potassium is important for nearly every physiologic function as a crucial constituent of the intracellular and extracellular fluid compartments. Potassium is essential for normal function of nervous, cardiac, and muscle tissue and plays a vital role in the renal, gastrointestinal (GI), and endocrine systems. Multiple regulatory systems operate concurrently to maintain potassium balance within precise physiologic limits in normal dogs and cats (Table 1). There are numerous pathologic processes and disease states that derange potassium homeostasis. Some of these are primary disorders of potassium balance, but others alter potassium balance indirectly as a consequence of a general pathologic change (secondary potassium disorders). As a result, potassium abnormalities are probably the most common—and most significant—of the electrolyte changes encountered in daily practice. For this reason, prompt recognition and correction of potassium imbalance in sick animals will reduce morbidity and improve treatment outcomes for many patients.

Potassium imbalance can occur in association with a large number of disorders, and complete discussion of each of these disorders is beyond the scope of this article. Two important primary potassium disorders, hypoadrenocorticism (Addison’s disease) and hyperaldosteronism (Conn’s syndrome), will be discussed in detail. Relevant general information about the clinical management of potassium imbalances will also be presented.

DIAGNOSTIC CRITERIA

Historical Information

Gender Predisposition
Overall, there is no gender predisposition for potassium disorders.
• Hypoadrenocorticism is reported to be more common in female dogs.
• Most cats diagnosed with hyperaldosteronism are male.

Age Predisposition
In general, the patient’s age is usually not helpful in determining the specific cause of potassium disorders.
• Diseases that lead to acute or chronic abnormalities of serum potassium tend to be more common in certain age groups (e.g., chronic renal failure in older cats).
• Hypoadrenocorticism is typically diagnosed in young dogs. The mean age at diagnosis is approximately 4.5 years; roughly 80% of dogs will be <7 years old at diagnosis.

Breed Predisposition
• The majority of hyperaldosteronism cases have been reported in cats, but it is a rare condition; hyperaldosteronism has been reported sporadically in dogs.

Editorial Mission
To provide busy practitioners with concise, peer-reviewed recommendations on current treatment standards drawn from published veterinary medical literature.

This publication acknowledges that standards may vary according to individual experience and practices or regional differences. The publisher is not responsible for author errors.

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KEY TO COSTS
$ indicates relative costs of any diagnostic and treatment regimens listed.
Cats and dogs can develop hypoadrenocorticism, but it is much more common in dogs. Overall, hypoadrenocorticism is an uncommon endocrinopathy.

Dogs of any breed can develop hypoadrenocorticism, although certain breeds appear to be more frequently affected than others. Standard poodles (specifically those with a black haircoat) are often cited as being predisposed to development of hypoadrenocorticism. Other breeds cited as at risk include Labrador retrievers, rottweilers, Great Danes, West Highland white terriers, and Portuguese water dogs.

The validity of the apparent breed predispositions is questionable because most cases of hypoadrenocorticism occur in non-purebred dogs.

Pseudohyperkalemia is a laboratory error detected in hemolyzed blood samples. It is most common in Akitas, which have a high potassium concentration in red blood cells.

**Owner Observations**

Owner observations of animals with potassium disorders are generally nonspecific; common complaints include lethargy and weakness. Polyuria and polydipsia can occur in association with hypokalemia (any cause).

**Hyperaldosteronism**

- Cats and dogs exhibit similar clinical signs.
- Signs are often episodic; a spectrum of vague signs can be reported.
- Polyuria.
- Polydipsia.
- Weakness.
- Nocturia is an unusual complaint in veterinary medicine that has been reported in several cats with hyperaldosteronism.
- Weight loss.
- Ataxia.
- Dysphagia.
- Vision loss/blindness.
- Exercise intolerance (reported in a dog with hyperaldosteronism).

**Hypoadrenocorticism**

- Signs are similar in dogs and cats.
Owners are often unaware that the pet is ill until a hypoadrenal crisis develops.

Owners often register vague complaints such as lethargy, decreased energy, and reduced activity level.

Signs range in severity from mild to life threatening.

- Anorexia.
- Weakness.
- GI complaints, such as vomiting/diarrhea/melena.
- Weight loss.
- Collapse.

**Other Historical Considerations/Predispositions**
The course of illness (acute versus chronic) suggests differential diagnoses for potassium abnormalities but is not a reliable diagnostic tool in every circumstance.

- Most primary potassium disorders are caused by endocrinopathies and should be considered when secondary causes of potassium imbalance have been ruled out.

- Hypoadrenocorticism in dogs can be part of an endocrinopathy characterized by multiple endocrine failures, probably from an immune-mediated mechanism (autoimmune polyglandular disease). Reported concurrent endocrinopathies include hypothyroidism, diabetes mellitus, hypoparathyroidism, and male reproductive failure.

**Physical Examination Findings**
Hypokalemia and hyperkalemia cause very few specific physical abnormalities.

**Hypokalemia of Any Cause**
- Muscle weakness, which can be marked.
- Cervical ventroflexion and inability to raise head is often observed with severe hypokalemia.
- Muscle weakness of any cause (e.g., myasthenia gravis) may produce similar signs, as can thiamine (vitamin B1) deficiency.
- Cervical ventroflexion due to hypokalemia is flaccid; that produced by thiamine deficiency is spastic.

**Hyperkalemia of Any Cause**
- Lethargy.
- Muscle weakness.
- Bradycardia.

**Hyperaldosteronism**
- Retinal detachment.
- Weakness (can be marked).
- Lethargy.
- Dehydration.

**Hypoadrenocorticism**
- Bradycardia.
- Diarrhea.
- Melena or hematochezia.
- Poor haircoat.
- Thin body condition.

- Marked hypovolemia.
- Abdominal pain.

**Laboratory Findings**
Potassium imbalance can occur in association with a large number of disorders (Table 2). Discussion of the laboratory abnormalities that accompany those disorders is beyond the scope of this article. Laboratory findings of primary potassium disorders are listed.

**Hyperaldosteronism**
- Hyperaldosteronemia: Usually marked.
- Hypokalemia: Marked.
- Hypernatremia.
- Hyperchloremia.
- Elevated blood urea nitrogen (BUN).

**Hyperglycemia**
- Elevated creatine kinase (CK) activity.
- Elevated alanine aminotransferase (ALT) activity.
- Alkalemia.
- Decreased magnesium.
- Decreased phosphorous.
- Elevated bicarbonate.
- Increased urinary potassium excretion.
- Increased fasting plasma renin level.

**Hypoadrenocorticism**
- Decreased sodium:potassium ratio. Values ≤27 are often cited as suspicious for hypoadrenocorticism; values ≤20 are more specific. A low Na/K ratio is not pathognomonic for hypoadrenocorticism because certain nonadrenal disorders (e.g., severe GI disease) can produce low Na/K ratios.
- Hyperkalemia can be marked (many dogs will have K+ concentration >7 mEq/L).
- Hyponatremia can be marked (many dogs will have Na+ concentration <130 mEq/L).
- No increase in serum cortisol level after adrenocorticotropic hormone (ACTH) injection.
- Mild anemia.
- Mild lymphocytosis, neutropenia, and thrombocytopenia; occasionally eosinophilia or basophilia.
- Mild hypercalcemia.
- Mild hypoglycemia.
- Azotemia.
- Hypochloremia.
- Hypocholesterolemia.
- Hypoproteinemia.

Animals with atypical hypoadrenocorticism may present with normal electrolyte concentrations. Even with normal electrolytes, an ACTH stimulation test should be performed to evaluate adrenal function in animals that have clinical signs that are consistent with hypoadrenocorticism.
Other Diagnostic Findings

Doppler Blood Pressure
- Hyperaldosteronism is consistently associated with hypertension (>180 mmHg) in cats.
- Animals presenting with a hypoadrenal crisis often have severe hypovolemia and marked hypotension.

Ophthalmic Examination
Retinal detachment and hemorrhage is reported in cats with hyperaldosteronism.

Electrocardiography
- Electrocardiography has low sensitivity and high specificity for hyperkalemia but is generally not helpful for the diagnosis of hypokalemia.
- Hyperkalemia of any cause can produce characteristic ECG changes, including:
  - Bradycardia.
  - Wide QRS complex.
  - Prolonged PR interval.
  - Absence of P waves.
  - Tented T waves.
- Hypokalemia of any cause can produce similar ECG changes:
  - Supraventricular and ventricular arrhythmias.
  - ST segment changes and decreased T wave amplitude can be observed but are inconsistent.
  - Prolonged QT interval and the appearance of the U wave have been observed with severe hypokalemia (dogs).

Radiography
- Radiography has low sensitivity and specificity for the diagnosis of primary potassium disorders.
- Hyperaldosteronism: Radiographic mass lesions can occasionally be detected in the area of the adrenal glands.
- Hypoadrenocorticism
  - Microcardia and a smaller than expected caudal vena cava, due to marked hypovolemia, is commonly observed but is a nonspecific finding.
  - Megaeosophagus may occur in association with profound muscle weakness.
  - Adrenal mass(es) can be observed in animals with hypoadrenocorticism caused by destructive lesions of the adrenal glands (rare).

Ultrasonography
- Hyperaldosteronism
  - Ultrasound examination is more sensitive than radiography for the detection of adrenal pathology.
  - Adrenal mass(es) are detected in most cases.
- Hypoadrenocorticism
  - Ultrasonography is generally not useful for the diagnosis of hypoadrenocorticism.
  - Finding that the adrenals are very small in size increases the suspicion for hypoadrenocorticism but can also be caused by prolonged glucocorticoid administration.
Summary of Diagnostic Criteria

- Laboratory confirmation of serum potassium levels below (hypokalemia) or above (hyperkalemia) the reference range is sufficient for diagnosis of a potassium disorder.

- Hyperaldosteronism
  - Hyperaldosteronemia in the absence of diseases that cause a secondary increase in aldosterone (e.g., heart failure).
  - Concurrent hypokalemia and hypertension, with appropriate clinical signs.
  - An adrenal mass is usually present in dogs and cats.

- Hypoadrenocorticism
  - The combination of hypocortisolemia and lack of adrenal response to stimulation by ACTH is diagnostic.
  - Hyponatremia with hyperkalemia (low Na/K ratio) is often present.

Differential Diagnoses

Potassium abnormalities occur as a secondary complication of many different diseases as well as a result of primary disorders of potassium homeostasis. The differential diagnoses for...
Hyperkalemia and hypokalemia are shown in Table 2. Common diseases and disorders associated with potassium abnormalities that resemble those caused by primary potassium disorders are discussed below.

**Hyperaldosteronism**
- Renal failure is differentiated by laboratory evaluation and response to IV fluid therapy.
- Normal ACTH stimulation with hypoaldosteronemia.

**Hypoadrenocorticism**
- Pseudohypoadrenocorticism: Affected animals have a normal ACTH stimulation.
- Severe GI disease: GI diagnostics, including fecal examination.
- Pregnancy: Documentation of pregnant state.
- Any cause of impaired renal potassium excretion.
  - Acute renal failure: Normal ACTH stimulation.
  - Obstructive uropathy (any cause).
  - Severe hypovolemia or other cause of marked reduction in renal blood flow.

**Iatrogenic Hyperkalemia**
- Excessive administration of potassium-containing drugs or fluids.
- Peritoneal/pleural fluid drainage.

**Factitious Hyperkalemia**
Laboratory artifact caused by thrombocytosis or hemolysis.

**TREATMENT RECOMMENDATIONS**

**Initial Treatment**
General treatments for potassium disorders are shown in Table 3. Specific therapy for primary potassium disorders is outlined below.

**Hyperaldosteronism**
- Restore normokalemia using potassium supplementation (see Table 3).
- Control hypertension.
- Adrenalectomy to remove aldosteronoma.

**Hypoadrenocorticism**
- Supportive care to reduce hyperkalemia (see Table 3).
- Mineralocorticoid supplementation:
  - Desoxycorticosterone pivalate (DOCP), 2.2 mg/kg IM every 21–30 days. Do not exceed a total dose of 50 mg/injection. Adjustments in the administered dose are made based on electrolyte concentrations (measured 10 to 14 days after the injection for the initial 2 to 3 injections), and the frequency is adjusted based on the duration of the injection. Dose adjustments, when made, are usually small changes (10% increase or decrease) and are reflected in the next injection (e.g., a dog that has hypokalemia on day 14 will receive 10% less DOCP at the next treatment). Most dogs will be controlled with a DOCP injection every 3 to 4 weeks.
  - Fludrocortisone, initial dose of 0.01 to 0.02 mg/kg PO once daily; adjust in increments of 0.05 to 0.1 mg per day as needed to control electrolyte abnormalities.
- Glucocorticoid replacement: Prednisone, 0.2 mg/kg PO to provide exogenous glucocorticoids if needed. Usually required when DOCP is used; may not be needed if fludrocortisone is used as this drug also has glucocorticoid activity. The dose of prednisone should be increased when stressful events are anticipated.

**Patient Monitoring**
- Serial determination of serum electrolytes is indicated for all animals treated for potassium disorders until the electrolytes are normal and the patient's condition is stable. Electrolytes should be measured every 6 to 24 hours depending on the patient's condition and the expected rate of change in the electrolytes.
• Resolution of clinical signs should accompany correction of electrolytes.
• ECG monitoring is important for assessment of hyperkalemic patients and during the treatment of hyperkalemia with calcium gluconate (see Table 3).
• Efficacy of mineralocorticoid treatment of animals with hypoadrenocorticism is monitored using serial measurements of serum sodium and potassium concentrations. Initially, electrolytes are monitored every 1 to 2 weeks. Once electrolyte concentrations are stable, monitoring every 3 months may be appropriate.

Home Management
Hyperaldosteronism and Hypoadrenocorticism
• Owner compliance with prescribed treatments must be encouraged to avoid recurrence of clinical signs.
• Owners must be educated about the expected clinical signs that may occur if treatment fails or the problem recurs.
• The need for periodic examination by a veterinarian must be emphasized, especially in animals with hypoadrenocorticism that must receive life-long therapy.

Milestones/Recovery Time Frames
Hyperaldosteronism
• Resolution of serum electrolyte and hormone abnormalities should occur within 24 to 36 hours following surgical removal of aldosteronoma.
• Resolution of clinical signs should parallel normalization of electrolyte concentrations.

Hypoadrenocorticism
• Dramatic improvement in clinical and laboratory abnormalities can be observed after volume replacement alone, but complete resolution will not occur until proper hormonal therapy is begun.
• Glucocorticoid therapy is responsible for alleviation of many of the most dramatic clinical signs (profound lethargy, GI signs, and vascular collapse).
• Electrolyte disturbances may not completely resolve until mineralocorticoid therapy is instituted.

Treatment Contraindications
Hypokalemia
• Potassium chloride is contraindicated as an oral potassium supplement because it is not well tolerated; use can cause vomiting and promote acidosis.

Hyperkalemia
• Potassium supplementation by any method is contraindicated if hyperkalemia is suspected or documented. Potassium-sparing diuretics are contraindicated.

PROGNOSIS

Favorable Criteria
• Correctable/reversible cause of hypo- or hyperkalemia.
• Hyperaldosteronism: Adrenal mass identifiable and amenable to surgical removal.
• Hypoadrenocorticism:
  — Rapid recognition and diagnosis of clinical signs.
  — Patient does not have renal failure.
  — Electrolyte concentrations readily controlled with mineralocorticoid supplementation.

Unfavorable Criteria
• Cause of hypo- or hyperkalemia is not reversible or readily treated.
• Treatment failure or poor response. Alternative therapy should be attempted if a patient fails to respond to initial therapeutic attempts.
• Hyperaldosteronism:
  — Patient is a poor surgical candidate.
  — Adrenal mass is not resectable or has invaded the caudal vena cava.
  — Irreversible or debilitating complications of hypertension occur (e.g., neurologic deficits).
• Hypoadrenocorticism:
  — Megasophagus does not resolve with hormone treatment or aspiration pneumonia is present.
  — Patient has renal failure.
  — Patient has secondary hypoadrenocorticism, which can be associated with less favorable prognosis than primary hypoadrenocorticism, depending on the initiating cause.
  — Poor control of electrolytes with medication.
  — Cost of treatment is prohibitive for the pet owner.

RECOMMENDED READING