Endocrinology – Brushing Up on Addison's Disease

Franziska Meyer, Dr. med. vet. DACVECC, FVH

Hypoadrenocorticism (Addison's disease) remains a diagnostically challenging and potentially life-threatening endocrinopathy in small animal medicine. Despite improved survival following the introduction of glucocorticoid therapy, affected patients continue to exhibit increased mortality rates compared to the general population. This review provides an advanced overview of the pathophysiology, clinical presentation, diagnostic approach, and therapeutic management of Addison's disease in dogs and cats, with emphasis on critical care considerations and recent insights into endocrine regulation.

Introduction and Historical Perspective

First described by Thomas Addison in 1855, primary adrenal insufficiency has evolved from a nearly uniformly fatal condition to a manageable chronic disease following the advent of cortisone therapy in the mid-20th century. Historically, one-year survival rates were below 20%; today, outcomes have improved significantly, though mortality remains elevated (1.5–5× higher than baseline). Contributing factors include both under-replacement and complications associated with glucocorticoid therapy.

Epidemiology

In dogs, hypoadrenocorticism has an estimated prevalence ranging from 0.06% to 0.5%, suggesting it is uncommon but likely underdiagnosed. A strong genetic predisposition exists in several breeds, including Standard Poodles, Portuguese Water Dogs, and Nova Scotia Duck Tolling Retrievers. Conversely, certain breeds (e.g., Golden Retrievers, Yorkshire Terriers) appear to have reduced risk.

Feline hypoadrenocorticism is rare, with fewer than 50 reported cases since 1983, limiting epidemiological conclusions.

Pathophysiology

Adrenal Hormone Function

Cortisol plays a central role in cardiovascular stability, metabolism, immune modulation, and stress response. Its absence results in impaired vascular responsiveness, decreased cardiac output, altered hematologic profiles, and metabolic dysregulation.

Aldosterone regulates sodium and potassium balance, as well as acid-base homeostasis. Deficiency leads to hyponatremia, hyperkalemia, and metabolic acidosis, which are hallmarks of primary hypoadrenocorticism.

Regulatory Axes

- Cortisol secretion is governed by the hypothalamic-pituitary-adrenal (HPA) axis via CRH and ACTH.
- Aldosterone secretion is primarily regulated by the renin-angiotensin-aldosterone system (RAAS) and serum potassium levels.

Classification of Hypoadrenocorticism

Primary Hypoadrenocorticism

- Most common form in dogs
- Typically immune-mediated destruction of the adrenal cortex
- Clinical signs manifest after ~85–90% cortical loss

Secondary Hypoadrenocorticism

- Due to pituitary dysfunction and decreased ACTH production
- Mineralocorticoid function often preserved

Tertiary / Iatrogenic Hypoadrenocorticism

- Rare or controversial in veterinary medicine
- May occur following chronic glucocorticoid administration

Clinical Presentation

Common Clinical Signs

- Lethargy, anorexia
- Vomiting, diarrhea (± melena or hematemesis)
- Weight loss, abdominal pain
- Polyuria/polydipsia
- Collapse or hypovolemic shock

Less Common Manifestations

- Hypoglycemia
- Seizures
- Megaesophagus

Clinicopathologic Findings

Characteristic abnormalities include:

- Hyponatremia and hyperkalemia (Na:K ratio < 27)
- Non-regenerative anemia
- Absence of stress leukogram (lymphocytosis, eosinophilia)
- Azotemia and hyperphosphatemia
- Metabolic acidosis
- Hypoglycemia, hypoalbuminemia, hypercalcemia

Electrocardiographic changes secondary to hyperkalemia may include:

- Peaked T waves
- Prolonged PR interval

- Absent P waves
- Ventricular arrhythmias or asystole

Diagnostic Approach

The gold standard diagnostic test is the ACTH stimulation test:

- Dogs: baseline and 1-hour post-stimulation cortisol measurement
- Cats: baseline, 60- and 90-minute measurements

Endogenous ACTH concentration aids in differentiating primary from central (secondary) disease.

Therapeutic Management

Emergency Stabilization of Addisonian crisis requires:

- Aggressive fluid resuscitation (preferably balanced crystalloids)
- Careful correction of hyponatremia
- Treatment of hyperkalemia (with caution when using insulin)
- Glucose supplementation as needed

Balanced crystalloids are preferred over isotonic saline due to improved potassium correction and reduced risk of rapid sodium shifts.

Symptomatic Therapy

- Antiemetics: ondansetron, maropitant
- Gastroprotectants: omeprazole, sucralfate
- Analgesia: opioids

Acute Phase Hormone Replacement Therapy

Hydrocortisone is preferred due to combined glucocorticoid and mineralocorticoid effects:

- CRI: 0.5–0.625 mg/kg/h
- Intermittent dosing: 1.25 mg/kg IV followed by maintenance dosing

Chronic Hormone Replacement Therapy

- **Mineralocorticoids**:
  - DOCP (desoxycorticosterone pivalate): 2.2 mg/kg SC every 28 days
  - Fludrocortisone: oral alternative, but may induce iatrogenic hyperadrenocorticism
- **Glucocorticoids**:
  - Prednisolone or dexamethasone at physiologic doses

Feline Hypoadrenocorticism

Although rare, feline Addison's disease should be considered in young cats presenting with collapse, dehydration, and weakness. Diagnostic protocols mirror those in dogs, though interpretation may require adjunctive imaging (e.g., adrenal gland size <2.7 mm).

Treatment typically includes:

- DOCP (often at higher starting doses than dogs)
- Low-dose prednisolone

Species-specific differences in glucocorticoid receptor density and affinity may influence therapeutic response.

Despite advances in diagnostics and therapy, hypoadrenocorticism remains the "great pretender" in veterinary medicine. Its nonspecific clinical presentation necessitates a high index of suspicion. Early recognition and appropriate management of adrenal crises are critical to improving outcomes.