



Dealing with the Addisonian crisis!

Hypoadrenocorticism (Addison's disease) is most commonly seen in the primary form¹. Primary hypoadrenocorticism is an immune mediated disease which causes destruction of the adrenal cortex. This destruction leads to a deficiency of both steroid hormones, glucocorticoids and mineralocorticoids.

Atypical hypoadrenocorticism occurs with a deficiency in glucocorticoids with normal mineralocorticoids. This form is less common and usually presents as a chronic disease, often with waxing and waning gastrointestinal signs, often at times of stress or illness.

Secondary hypoadrenocorticism is caused by reduced ACTH secretion from the pituitary gland due to negative feedback secondary to iatrogenic steroid supplementation (prednisolone), or destruction of the pituitary secretory tissues (neoplasia).

As the disease can be an imitator of many others, an awareness of the classic clinicopathological findings and typical signalment can increase the likelihood of diagnosis.

This topic focuses mainly on primary Addison's disease.



Anatomy and physiology of the adrenal gland

The adrenal glands are endocrine organs which are bilaterally located in an anterior position to the kidneys. The glands are made up of two separate sections, the cortex and the medulla. Steroid hormones such as cortisol, corticosterone, aldosterone and sex hormones are produced in the adrenal cortex while the medulla produces epinephrine and norepinephrine.

An important mineralocorticoid called aldosterone is produced in the adrenal cortex. Aldosterone is responsible for sodium reabsorption and potassium excretion in the distal renal convoluted tubule and collecting duct. Without aldosterone, an altered electrolyte and water homeostasis develops, leading to hypovolaemia, hypotension, hyperkalaemia and hyponatraemia. Hyponatraemia decreases the osmotic pressure of plasma which also causes fluid to shift out of the vascular space leading to hypovolaemia and hypotension⁶.

The main glucocorticoid is cortisol which is responsible for many aspects of metabolism such as the conversion of amino acids to carbohydrates³. It also plays a role in gastrointestinal function, mentation and appetite.

Signalment

Young to middle aged (4-6 years) female dogs, although it can be seen at any age⁵.

Overrepresented breeds of the dog include the Standard Poodle, Portuguese Water Dog, Nova Scotia Duck Tolling Retriever, Bearded Collie, Rottweiler, and WHWT². The disease is rare in cats.

Presenting signs

The disease can present in many forms, with some patients suffering mild chronic waxing and waning signs and others present with acute life-threatening disease. Addison's disease may cause the following clinical signs:

- Lethargy
- Polyuria
- Polydipsia
- Vomiting
- Diarrhoea



- Anorexia
- Weight loss
- Muscle weakness
- Collapse
- Dehydration
- Bradycardia despite collapse and dehydration

The patient must lose 90% of adrenal function before displaying signs of the disease.

Clinical Findings

Hyperkalaemia and hyponatraemia are hallmark signs of mineralocorticoid deficiency.

- **Hyperkalaemia** – slows down the pacemaker activity of the heart and decreases sensitivity of conductive tissue resulting in bradycardia¹.
ECG – progressive hyperkalaemia causes tall spiked T waves, followed by depressed or even absent P waves (atrial standstill), then progressive widening of the QRS complex and eventually ventricular fibrillation or ventricular asystole⁶.

Signs -bradycardia, dysrhythmias with serum potassium levels $>6.5\text{mmol/L}$ ¹. Note: *bradycardia in the face of hypovolaemia is inappropriate and should alert one to the possibility of Addison's disease.*

- **Hyponatraemia** – prerenal azotaemia may occur due to dehydration alongside hyponatraemia. This can be difficult to differentiate between acute renal failure and Addison's disease¹. An ACTH stimulation test should be performed in these cases, especially in younger patients.
- **Hypoglycaemia** – cortisol acts as an insulin antagonist and is responsible for the conversion of amino acids to carbohydrates which typically has a hyperglycaemic effect. Cortisol deficiency can cause a mild hypoglycaemia.
- **Isothenuria** – a urine specific gravity of $<1.030\text{g/dl}$ was noted in 60-88% of Addisonian dogs⁴.
- **Hypercalcaemia and hypochloraemia** due to hypoaldosteronaemia.
- **Haematological abnormalities** include non-regenerative anaemia, neutropaenia, lymphocytosis, and eosinophilia (reverse stress leukogram). Note a *reverse stress leukogram in an unwell patient is inappropriate and can be an indicator of Addison's disease.*



Initial stabilisation

Emergency treatment should be administered to correct hypovolaemia, metabolic acidosis, hypoglycaemia and electrolyte abnormalities².

Hypovolaemia

In an Addisonian crisis, normal saline 0.9% should be administered at shock rate of 90ml/kg^2 . The patient's hydration status should be reassessed after each 10ml/kg bolus by checking

pulse quality, CRT, heart rate and blood pressure. This is essential during rapid fluid therapy resuscitation.

Fluid therapy to correct hypovolaemia will promote renal diuresis and encourage potassium excretion.

Immediate blood sampling for an ACTH stimulation test is essential for rapid diagnosis to initiate treatment options.

Hypoglycaemia can be treated with a 50% dextrose solution as a bolus or CRI as required.

Dexamethasone (Dexadrenon®) should be administered 0.25-1.0mg/kg IV. This is the only glucocorticoid which will not interfere with the ACTH result however, administration after the second cortisol blood sample is preferable².

Sodium retention should be monitored when administered rapidly alongside mineralocorticoids to avoid an overcorrection of hyponatraemia.

Severe hyperkalaemia (>7.5mmol/L) if this is persistent and not correcting with fluid resuscitation, other treatment may be required¹:

- Calcium gluconate 10% (0.5-1.5ml/kg) may be administered slowly IV while ECG monitoring, if available. This helps restore normal cardiac conduction and stabilise myocytes¹.
- Neutral insulin (0.2-0.5iu/kg) can be administered IV to stimulate cellular uptake of potassium and rapidly reduce hyperkalaemia.
- Dextrose solution should be administered IV alongside the neutral insulin to prevent hypoglycaemia.



Diagnosis

An ACTH stimulation test should be performed as soon as the disease is suspected. A basal sample is taken before administering synacthen 0.005mg/kg IV and a post sample is taken one hour later. Addisonian patients have consistently low basal and post ACTH cortisol concentrations (<5 µm/ml). Always check that the patient has not received any exogenous glucocorticoids prior to the test, as they suppress ACTH secretion from the anterior pituitary gland.

A Na:K (divide sodium value by the potassium value) can be calculated to help diagnose Addison's disease.

Results <27 are abnormal, <24 suggestive and <21 are highly suggestive of the disease. Other causes of a low Na:K include severe whipworm infestation and pleural effusions.

Treatment

Maintenance therapy includes fludrocortisone acetate (Florinef®) at 0.02 mg/kg/day PO, as a mineralocorticoid supplement. Dose ranges may vary wildly between individuals and response can be monitored using weekly blood electrolyte concentrations (ideally patients should have Na:K >27). Glucocorticoid supplementation is indicated initially and during times of stress, but is used long term in less than 50% of patients. Prednisolone at 0.25 mg/kg PO BID as an initial dose, then tapered over 3-4 weeks until it can be discontinued.

Desoxycortone pivalate (DOCP) (Zycortal®) is a pure mineralocorticoid which can be administered via subcutaneous injection (2.2mg/kg) every 4 weeks. This must be administered alongside glucocorticoids such as prednisolone (0.2-0.4mg/kg PO SID).

Electrolytes should be repeated 10 days post initial treatment and again at 28 days to monitor treatment response and duration.

Prognosis

With successful medical management and good owner compliance, hypoadrenocorticism has an excellent prognosis².

Reference

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Biography

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Sophie qualified as a registered veterinary nurse in the United Kingdom in 2011. Since then she has worked in many different practices across the north west of England gaining essential veterinary experience.

Currently working at a specialist referral hospital in Frodsham, England - Northwest Veterinary Specialists LTD, she has practiced there for 4 years as a nurse team leader of the small animal internal medicine department.

After recent AIMVT exams in Washington DC, Sophie became a Veterinary Technician Specialist in Small Animal Internal Medicine.

Sophie's areas of interest are endocrinology and emergency medicine.

