Improve Veterinary Education

Addison's Disease in Dogs

Introductory summary

This handout explains adrenal physiology and the consequences of glucocorticoid and mineralocorticoid deficiency, highlighting typical and atypical canine Addison's disease, rare feline presentations, diagnostic pathways using basal cortisol and ACTH stimulation, and acute and long-term management strategies.

Introduction

This session addresses hypoadrenocorticism (Addison's disease) in dogs, with a brief consideration of cats. Addison's disease is particularly rewarding to diagnose and treat because it can present in non-classical ways; recognising these cases improves outcomes and clinical confidence. The aim is to strengthen clinicians' ability to identify both typical and atypical presentations and to apply a structured diagnostic and therapeutic approach.

Adrenal physiology and hormone production

A clear understanding of adrenal anatomy and function underpins clinical reasoning in Addison's disease. The adrenal gland consists of a medulla and a cortex. The cortex is organised into three functional zones. The zona glomerulosa produces aldosterone, which regulates electrolyte balance, principally sodium and potassium, and contributes to acid–base regulation. The zona fasciculata produces glucocorticoids; although their systemic actions are extensive, key functions emphasised here include maintenance of blood pressure, support of gastrointestinal tract integrity, and an essential role in gluconeogenesis. The zona reticularis contributes to sex hormone production. The medulla produces epinephrine (adrenaline) and norepinephrine (noradrenaline), hormones central to fight-or-flight responses.

Pathophysiology of Addison's disease

The clinical syndrome of Addison's disease reflects the loss of hormones normally produced by the adrenal cortex. Glucocorticoids exert broad physiological effects and a small baseline level is essential for survival. They support gluconeogenesis and thereby contribute to glucose production, and they help maintain blood pressure by influencing receptor-mediated vascular tone. Their effects on the gastrointestinal tract are clinically important, particularly in

maintaining mucosal function. This explains why some dogs with Addison's disease may develop ulcerative lesions: without adequate glucocorticoid activity, gastrointestinal mucosal health is compromised. Mineralocorticoid deficiency, specifically loss of aldosterone activity, disrupts sodium absorption and potassium excretion and contributes to acid–base abnormalities; the hallmark biochemical pattern is hyponatraemia with hyperkalaemia.

Primary and secondary hypoadrenocorticism

Hypoadrenocorticism may be primary or secondary, although primary disease is often assumed by default. In dogs, most cases are primary and result from destruction of the adrenal cortex, most commonly through an autoimmune process. Less commonly, adrenal destruction may occur secondary to neoplasia or granulomatous disease. Not all Addisonian patients have definitive ultrasonographic abnormalities, yet abdominal ultrasonography can be valuable when the presentation is atypical or does not fit well with an autoimmune pattern, particularly to exclude infiltrative disease. Secondary hypoadrenocorticism is less common and may occur with pituitary or brain lesions. Endogenous adrenocorticotrophic hormone (ACTH) assists differentiation: in primary disease, endogenous ACTH is expected to be high due to loss of negative feedback, whereas in some secondary cases ACTH may be low. Measuring endogenous ACTH is reasonable in all patients and is particularly useful in atypical presentations or in patients with neurological signs, while maintaining awareness that most cases remain primary.

Typical and atypical Addison's disease in dogs

Typical Addison's disease involves combined glucocorticoid and mineralocorticoid deficiency, producing clinical signs attributable to both, including the classic electrolyte disturbances of hyponatraemia and hyperkalaemia. A frequently cited signalment is a young to middle-aged spayed female, typically around four to five years of age, with females overrepresented compared with males. Certain breeds are discussed more often, including Poodles and West Highland White Terriers, but the disease can occur in any breed.

Atypical Addison's disease is increasingly recognised and the term is being reconsidered because the phenotype is not truly rare. In this context, atypical disease refers to patients with hypoadrenocorticism who are eunatraemic and eukalaemic, with sodium and potassium within reference intervals. Some of these patients have low aldosterone, yet renal adaptive mechanisms can temporarily maintain electrolyte balance without mineralocorticoid supplementation. Importantly, a clinically meaningful proportion of these dogs progress along a continuum: they may initially present with eunatraemic/eukalaemic hypoadrenocorticism and later develop the classic electrolyte pattern of low sodium and high potassium, sometimes

within weeks. Endogenous ACTH can help refine expectations; markedly increased ACTH supports primary disease, whereas low ACTH in a case with neurological features would increase suspicion of secondary hypoadrenocorticism, in which electrolyte derangements may be less likely to develop and glucocorticoid replacement alone may be sufficient.

The proportion of atypical cases is often cited as approximately 20–34% depending on the population studied. In referral internal medicine practice, the perceived proportion may be higher because many such patients present as outpatients with chronic gastrointestinal signs. Increased testing and heightened awareness are expected to increase case detection over time. Atypical or chronic presentations tend to involve older dogs, often six to seven years of age, partly because signs may be less dramatic and can remain untreated for prolonged periods. Gastrointestinal signs predominate, with vomiting most common, alongside diarrhoea and a waxing-and-waning clinical course that can be frustrating for owners. Hypoalbuminaemia may be present. Some patients later develop classical electrolyte changes and require desoxycorticosterone pivalate (DOCP) injections. Once a eunatraemic/eukalaemic case is diagnosed, electrolyte monitoring should continue, for example every three months initially and subsequently every six months, with owners advised to report recurrence of vomiting or diarrhoea even if the patient is receiving steroids, as progression to mineralocorticoid dependence can occur.

Feline hypoadrenocorticism

Addison's disease is rare in cats, but clinicians should remain alert to the possibility. An illustrative case involves a cat managed with Addison's disease that attends monthly because the owners do not administer injections at home. The cat initially presented to an emergency service with profound lethargy and bradycardia. Triage testing revealed marked hyperkalaemia and increased renal values. Because the patient was a male cat, the initial assumption was urinary obstruction, leading to immediate catheter placement and fluid therapy. Despite relief of obstruction and evidence of substantial urine production, the electrolyte pattern remained inconsistent with urinary obstruction alone, prompting consideration of alternative diagnoses such as acute kidney injury and hypoadrenocorticism. An ACTH stimulation test was subsequently performed and confirmed Addison's disease. Published feline cases commonly describe electrolyte disturbances and often involve older cats. Although uncommon, feline hypoadrenocorticism should be included in differential diagnoses when clinical and biochemical patterns raise concern.

Clinical presentation: crisis and chronic/intermittent disease

Canine Addison's disease typically presents in two broad patterns. The first is an Addisonian crisis, characterised by an acute, severe presentation through emergency services. These patients are markedly weak, may collapse, are often dehydrated, and commonly vomit; haemorrhagic diarrhoea may occur. Clinical deterioration can be rapid over 24–48 hours. The second pattern is a chronic or intermittent presentation, in which signs fluctuate over time. Patients may have reduced appetite, be consistently fussy eaters, and experience episodic vomiting and diarrhoea followed by apparent recovery and subsequent relapse. This waxing-and-waning pattern contributes to the reputation of Addison's disease as "the great pretender". Many patients exhibit polyuria and polydipsia (PU/PD), frequently related to impaired urine concentrating ability associated with medullary washout. Tremors or shaking may be observed; in such cases, electrolyte assessment is essential because electrolyte imbalance, including that due to Addison's disease, may be contributory.

Physical examination findings

Physical examination findings vary with severity. In more severe presentations, dehydration may be evident through tacky mucous membranes and sunken eyes, alongside lethargy and signs of true hypovolaemic shock with hypotension. In critically ill patients, heart rate may be inappropriately low due to hyperkalaemia; heart rate should therefore be assessed carefully, and an electrocardiogram (ECG) should be obtained when hyperkalaemia is present. Melena may occur and is consistent with the combined effects of hypovolaemia and impaired gastrointestinal mucosal health secondary to glucocorticoid deficiency. In other cases, physical findings may be vague and patients may be referred for evaluation of chronic enteropathy and chronic vomiting.

Laboratory patterns and diagnostic pitfalls

Characteristic biochemical abnormalities include hyperkalaemia and hyponatraemia, which may be mild and fall near the limits of reference intervals rather than being extreme. Many patients are azotaemic, with creatinine often less than approximately 4 mg/dL, and may be isosthenuric. These features can lead to misdiagnosis as chronic kidney disease because patients cannot concentrate urine, a consequence of hormonal and electrolyte disturbances and medullary washout. Mild hypoglycaemia may be present. Hypercalcaemia, including changes detected on ionised calcium analysis, may also occur. In chronic or eunatraemic/eukalaemic presentations, hypoalbuminaemia and hypercholesterolaemia are reported more frequently; Addison's disease

should therefore remain a key differential diagnosis in dogs with enteropathy and low albumin, and clinicians should actively exclude it.

Haematological assessment may or may not show anaemia. A particularly informative clue is the absence of an expected stress leucogram in a markedly unwell patient; a severely ill animal without the anticipated stress pattern on a complete blood count should prompt consideration of Addison's disease among other differentials.

Although the sodium-to-potassium ratio is often discussed, it cannot reliably rule in or rule out Addison's disease when used in isolation and may encourage diagnostic anchoring. A more robust approach is to test any dog with hyponatraemia and hyperkalaemia, even when changes are mild, and to consider Addison's disease in dogs with chronic enteropathy even when electrolytes are normal. In practice, when submitting gastrointestinal panels measuring cobalamin, folate, and trypsin-like immunoreactivity (TLI), it is reasonable to include basal cortisol to avoid missing atypical hypoadrenocorticism.

Basal cortisol screening and the ACTH stimulation test

An ACTH stimulation test is not mandatory in every patient at first presentation if clinical suspicion is low. Basal cortisol can be used as a screening tool, particularly in chronic enteropathy investigations. A basal cortisol concentration greater than 2 µg/dL effectively rules out Addison's disease in this context. If basal cortisol is less than 2 µg/dL, an ACTH stimulation test is required to confirm or refute the diagnosis. Most dogs with Addison's disease have basal cortisol less than 1 µg/dL, and a smaller proportion, approximately 2%, fall between 1 and 2 µg/dL. When a dog presents with a classical Addisonian crisis and suspicion is high, clinicians should not delay definitive testing while awaiting send-out basal cortisol results; proceeding directly to ACTH stimulation testing is preferred where feasible.

Conduct of the ACTH stimulation test and steroid considerations

For ACTH stimulation testing, use of standard intravenous cosyntropin (rather than compounded preparations) is recommended. The stated dose is 5 µg/kg intravenously. Although lower-dose protocols have been studied, continued use of 5 µg/kg is justified on the basis that Addison's disease is a lifelong diagnosis and long-term therapy requires diagnostic certainty. Blood should be collected for pre-ACTH cortisol measurement, cosyntropin administered intravenously, and a second blood sample collected exactly one hour later for post-ACTH cortisol. A practical approach is to use a butterfly catheter to collect the baseline

sample, administer cosyntropin through the same access, flush with saline, wait one hour, and then collect the post-stimulation sample.

Prior to testing, it is essential to confirm that the patient is not receiving steroids that could suppress the hypothalamic–pituitary–adrenal axis and lead to misdiagnosis. While prednisone and dexamethasone are frequently remembered, budesonide and fluticasone can also suppress the axis and must be considered. If cosyntropin is unavailable but the presentation is strongly consistent with an Addisonian crisis, a single dose of dexamethasone sodium phosphate may be administered; dexamethasone is not measured as cortisol in most assays, so a single dose is unlikely to materially compromise interpretation, although multiple doses may begin to affect results. In such situations, testing should be performed as soon as possible. When sending samples to the laboratory, tubes should be clearly labelled as pre-ACTH and post-ACTH. If the laboratory is closed, serum can be frozen and submitted when services resume.

Storage and cost-saving strategies for cosyntropin

Cosyntropin is costly, and efficient use can reduce wastage. Where multiple patients require testing in a single day, one vial may be shared within that day's clinical workflow. If a vial is opened for one patient and surplus remains, the remainder may be stored by transferring it into plastic syringes as aliquots and freezing. Frozen aliquots can be kept for approximately six months under typical hospital protocols and thawed rapidly when needed. An example calculation illustrates the approach: at a concentration of 250 µg/mL, a 10 kg dog dosed at 5 µg/kg requires 50 µg, corresponding to 0.2 mL. The remaining volume can be divided into multiple 0.2 mL aliquots for future use. If a smaller dog requires 0.1 mL, one 0.2 mL aliquot can be thawed, 0.1 mL administered, and the remainder discarded, with charging structured per aliquot as appropriate.

An illustrative missed case: diagnostic anchoring and medullary washout

A representative non-classical case underscores the importance of integrating electrolytes with renal indices and urine concentrating ability. The patient had a history of nasal aspergillosis and presented with intermittent episodes of vomiting and diarrhoea. During episodes the dog stopped eating completely, and episodes typically lasted three to four days before self-resolving. At the primary practice, supportive care with subcutaneous fluids and an anti-emetic injection of maropitant resulted in marked improvement, yet episodes recurred. The owner reported increased drinking and urination and denied dietary indiscretion, emphasising the dog's selective appetite.

Initial in-house testing demonstrated a sodium concentration of 137, interpreted as mildly low, and a potassium concentration of 4.5, within reference limits but trending. Given the presence of diarrhoea and dehydration, hyponatraemia seemed potentially explicable. In view of PU/PD, urine was submitted for culture, and urine specific gravity was 1.014. At that stage, the working diagnosis was non-specific gastroenteritis with possible stage II chronic kidney disease, supported by azotaemia and isosthenuria. The key error was failing to recognise that the apparent renal phenotype could be driven by medullary washout associated with hypoadrenocorticism and that electrolytes required careful ongoing reassessment.

One week later, the dog returned substantially more unwell, with persistently increased renal values and an electrolyte profile consistent with classic Addison's disease, described here as hyperkalaemia with hyponatraemia. The diagnosis then became straightforward. This sequence highlights that urine specific gravity is informative but must not distract from electrolyte interpretation, and that apparent chronic kidney disease may in fact reflect endocrine-driven concentrating defects.

Acute stabilisation and emergency management

In suspected Addisonian crisis or in markedly unwell patients with supportive biochemical changes, priorities include correction of dehydration, assessment and correction of hypotension where present, and symptomatic management of nausea and gastrointestinal distress. In such cases, an ACTH stimulation test should be initiated immediately rather than awaiting basal cortisol results. Hyperkalaemia has important differentials, including urinary obstruction and extensive haemolysis, among other conditions; appropriate evaluation should proceed in parallel to avoid premature closure.

Glucocorticoid therapy is indicated promptly once diagnostic sampling permits. In the described approach, dexamethasone is administered immediately after collection of the post-ACTH sample when clinical suspicion is high, as the delay is only one hour. Mineralocorticoid replacement with DOCP is deferred until ACTH stimulation results are available. During the interim, fluid therapy assists stabilisation of electrolytes.

Fluid therapy: selection, calculation and monitoring

Fluid therapy aims to restore circulating volume and correct dehydration. In hypotensive patients or those with moderate to severe dehydration, an initial bolus of approximately 20 mL/kg is administered and deducted from the calculated deficit. Rehydration is then planned by

combining the remaining deficit with maintenance requirements. Electrolytes should be reassessed every four to six hours to evaluate trends while awaiting ACTH stimulation results.

Where choice exists, 0.9% sodium chloride is avoided in preference to balanced crystalloids. The reasoning is that 0.9% sodium chloride contains a sodium concentration of approximately 154 mEq/L; in patients whose serum sodium may be around 120–130, the sodium gradient between fluid and blood can be substantial. Rapid increases in serum sodium risk neurological injury. Balanced solutions such as lactated Ringer's solution (often referred to as Hartmann's solution), Plasma-Lyte, or Normosol-R contain sodium concentrations closer to physiological levels, typically in the region of 130–140, and include only small amounts of potassium, making them preferable in this context.

If clinically significant hypoglycaemia occurs with weakness, ataxia, or seizures, dextrose supplementation is added. Although Addisonian dogs commonly exhibit hypoglycaemia, it is usually mild; nevertheless, if severe hypoglycaemia is encountered, commencing with approximately 2.5% dextrose in fluids is described as an appropriate starting point.

Hyperkalaemia management and ECG-guided escalation

When biochemistry results are available, potassium concentration should be assessed immediately. ECG abnormalities become more likely at potassium concentrations above approximately 6.5–7 mEq/L; early changes include diminution of the P wave, with progressive abnormalities thereafter. Heart rate should be monitored closely, with particular attention to bradycardia. In many dogs with potassium around 6.5, patients remain clinically stable, and intravenous fluids are often sufficient to improve electrolyte balance. If potassium exceeds 7 mEq/L and bradycardia or other ECG abnormalities are present, escalation of therapy is warranted. Calcium gluconate may be administered to stabilise the myocardium. Potassium can be shifted intracellularly using dextrose with insulin; caution is advised because Addisonian patients may be hypoglycaemic, so dextrose should be administered first, using 50% dextrose diluted 1:1, followed by insulin at approximately 0.25 units/kg as a single dose. Patients should then remain on a dextrose infusion and blood glucose should be monitored frequently, for example every 30 minutes for several hours, to detect and manage hypoglycaemia. An alternative that may work well is the use of a beta-agonist, such as terbutaline at approximately 0.01 mg/kg intramuscularly, administered using an insulin syringe, or inhaled albuterol, with the aim of reducing serum potassium.

Steroid selection in acute disease and transition to oral therapy

Several glucocorticoid options are described as yielding similar clinical outcomes, including hydrocortisone continuous rate infusion, intravenous prednisolone, and dexamethasone sodium phosphate. One dose of dexamethasone, in the range of 0.1–0.15 mg/kg, is described as unlikely to cause major interference when administered after appropriate sampling. Supportive care accompanies steroid therapy, including rehydration, maropitant, and pantoprazole where there is evidence of gastrointestinal ulceration. Once patients are eating, therapy is transitioned to oral steroids. A typical starting oral prednisone dose is 0.5 mg/kg once daily until discharge, followed by tapering to the lowest effective daily dose.

Mineralocorticoid replacement: DOCP dosing, intervals and monitoring strategies

Mineralocorticoid replacement can be delivered using DOCP. Although the labelled dose is 2.2 mg/kg, a reduced dose of approximately 1.6 mg/kg is described as being supported by more recent publications and is used routinely. Subsequent management should be individualised. One monitoring strategy is to assess sodium and potassium at week four and then weekly thereafter until electrolytes begin to trend abnormal, at which point the interval between injections is identified; a practical illustration describes giving the first injection on 1 January, checking electrolytes at two weeks, then at four weeks on 1 February, and continuing weekly checks until mild hyponatraemia and hyperkalaemia emerge, indicating that the patient requires a shorter interval, for example five weeks. An alternative approach prioritises adherence by maintaining a monthly schedule and reducing dose in increments, for example by approximately 20%, until electrolytes remain stable; this method aligns with other routine monthly preventative treatments and may be easier for owners to remember. Both approaches are considered acceptable, and some patients ultimately require intervals of six to eight weeks.

Chronic glucocorticoid dosing, stress dosing and long-term expectations

For chronic glucocorticoid therapy, prednisone is tapered to the lowest effective daily dose. Some dogs, particularly large dogs, require very small doses and can be tapered down to approximately 0.05 mg/kg once daily while remaining clinically stable. Stress dosing remains important; during stressful events, such as a veterinary visit in an anxious patient, the daily dose is doubled for that day. Ongoing adjustments may involve modifying dose or injection intervals to maintain clinical stability and normal electrolytes.

Troubleshooting and blood pressure considerations

Persistent PU/PD and polyphagia despite therapy commonly indicate excessive glucocorticoid dosing; clinicians should ensure the patient is receiving the lowest effective dose once daily. Blood pressure should be measured and managed appropriately, because both DOCP and steroid therapy can contribute to hypertension, and some patients become hypertensive during treatment. Dose adjustments should be made in response to clinical signs, blood pressure, and electrolyte monitoring.

Case example: Dug

A practical example illustrates management outside a classic crisis. Dug was approximately 5% dehydrated and vomiting at home, with a normal heart rate, a normal ECG, and normal blood pressure, indicating a clinically unwell patient rather than a fulminant Addisonian crisis. The dog weighed approximately 20 kg. Management included fluid therapy to correct dehydration plus maintenance requirements, a single dose of dexamethasone at approximately 0.15 mg/kg and maropitant, with an ACTH stimulation test performed before dexamethasone administration. The following day the dog was clinically improved. The patient was discharged on prednisone, described as 10 mg daily for five days, then reduced to 5 mg, and subsequently to 2.5 mg once daily. DOCP was initiated at approximately 1.6 mg/kg. Over time, the injection interval was increased, and the patient ultimately did well on an interval of approximately eight weeks.

Conclusion

Not every Addisonian patient presents as a classic crisis case. Addison's disease should be considered in any dog with vomiting, and a basal cortisol measurement should be incorporated into the work-up of chronic vomiting and chronic enteropathy to avoid missing atypical disease. Although long-term therapy is required, prognosis is excellent and these cases can be particularly rewarding to manage.