When Addison's is a crisis: Adrenal FAQs

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Conflicts of Interest & Disclaimer

+ Stephanie Sorrell is an employee of IDEXX Laboratories UK

+ Yvonne McGrotty is an employee of IDEXX Laboratories UK and also an employee of AniCura France.

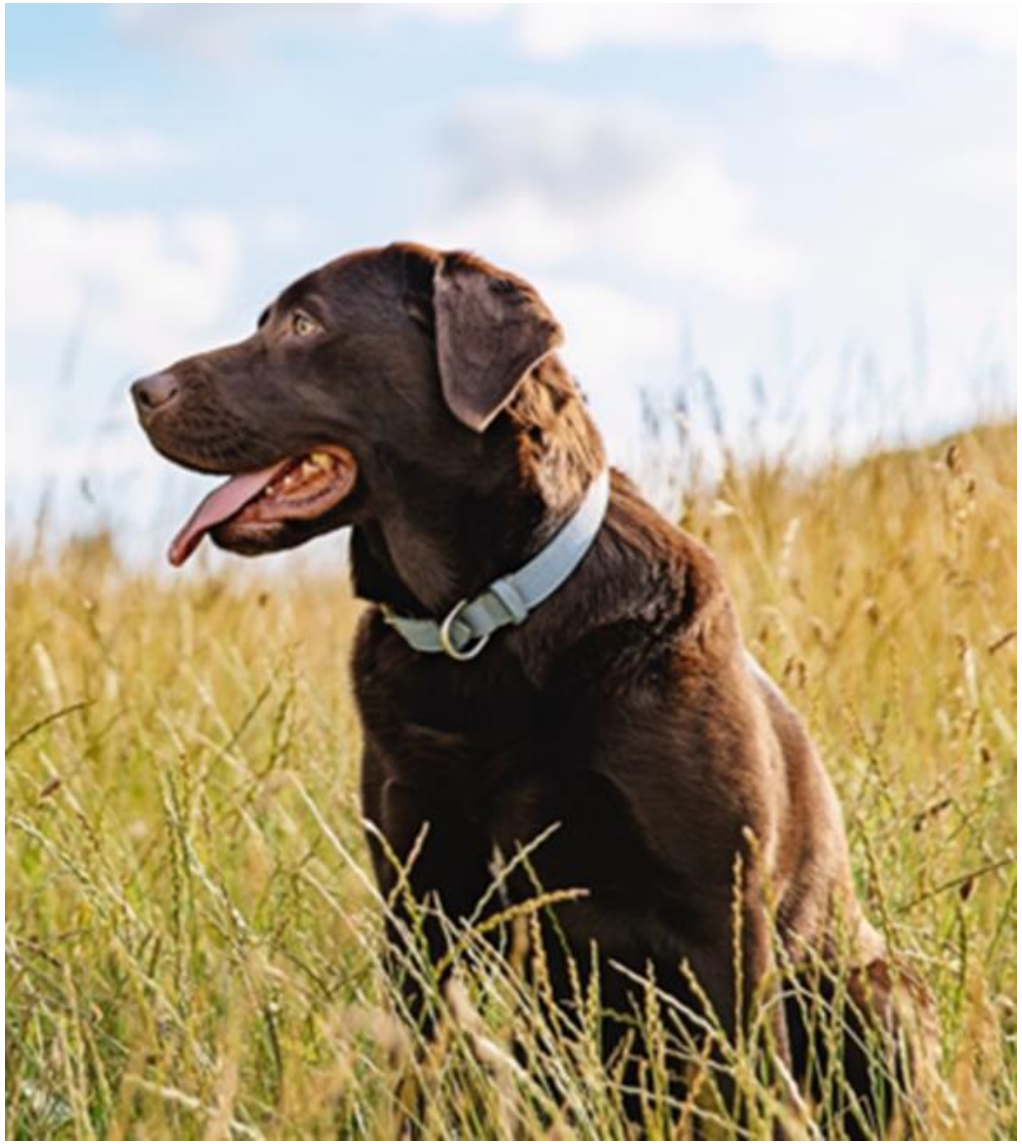
+ *The information contained herein is intended to provide general guidance only. As with any diagnosis or treatment, you should use clinical discretion with each patient based on a complete evaluation of the patient, including history, physical presentation, and complete laboratory data. With respect to any drug therapy or monitoring program, you should refer to product inserts for a complete description of dosages, indications, interactions, and cautions. Diagnosis and treatment decisions are the ultimate responsibility of the primary care veterinarian.*

What is hypoadrenocorticism?

Hyponatremic and/or hyperkalemic hypoadrenocorticism

- This is defined as hypoadrenocorticism with hyperkalemia and/or hyponatremia.
- This is due to primary hypoadrenocorticism.
- This form has previously been referred to as typical hypoadrenocorticism

*ESVE Alive definition



Eunatraemic, eukalaemic hypoadrenocorticism

- This is defined as hypoadrenocorticism with normal serum concentrations of potassium and sodium.
- This could be due to primary or secondary hypoadrenocorticism.
- This form has previously been referred to as atypical hypoadrenocorticism

*ESVE Alive definition

What screening test can be used for hypoadrenocorticism?

Basal cortisol as screening test

+ Basal cortisol >55nmol/L makes hypoadrenocorticism unlikely

- In dogs with chronic enteropathy at referral, hypoadrenocorticism is an uncommon cause of signs
  - 28% dogs (79/282) had basal cortisol <55nmol/L
  - However, only 1 of 282 dogs had a final diagnosis for hypoadrenocorticism

Gallego AF, Gow AG, Boag AM. Evaluation of resting cortisol concentration testing in dogs with chronic gastrointestinal signs. J Vet Intern Med. 2022 Mar;36(2):525-531. doi: 10.1111/jvim.16365. Epub 2022 Feb 3. PMID: 35118742; PMCID: PMC8965248.

Can I use LDDST to screen for hypoadrenocorticism?

LDDST as screening test

- No not suitable for testing for hypoadrenocorticism either as screening or confirmation
- Useful only for testing for hyperadrenocorticism

What does it mean if I test for Addison’s and the post ACTH cortisol is elevated?

ACTH stimulation test

ENDOCRINOLOGY

ALERT	TEST	RESULT	UNITS	REF.INTERVAL
High	*Cortisol - Baseline	203.0	nmol/L	25.0 - 125.0
High	*Cortisol - Post ACTH	910.0	nmol/L	125.0 - 520.0

- Do not overinterpret
- If a patient does not have clinical signs of hyperadrenocorticism it is very unlikely to be a true positive
- False positives are common

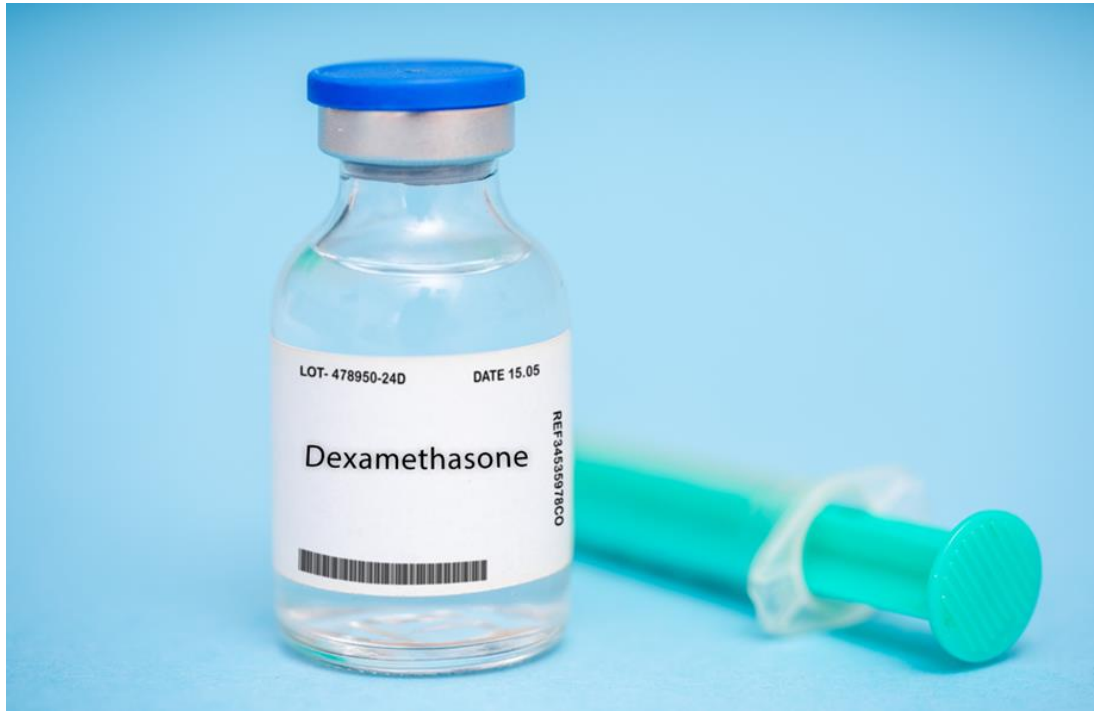
Do steroids affect testing for Addison’s disease?

Effect of steroids

+ Steroids will reduce basal cortisol and ACTH stimulation test results and results can mimic hypoadrenocorticism

+ Dexamethasone does not cross react with cortisol assay at lab testing so can be given within 24hour of testing

+ Dose/duration of steroid use will affect length of cortisol suppression



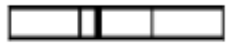
What changes on routine haematology and biochemistry can be consistent with “typical” hypoadrenocorticism?

Consistent signs

+ Lack of stress leukogram
+ Hypoglycaemia
+ Azotaemia
+ Hyponatraemia, hypochloraemia, hyperkalaemia
+ Hypercalcaemia

Investigations

HAEMATOLOGY

ALERT	TEST	RESULT	UNITS	REF.INTERVAL	
	*RBC	7.12	10^12/L	5.39 - 8.70	
	*Haematocrit	0.529	l/L	0.383 - 0.565	
	*Haemoglobin	18.0	g/dL	13.4 - 20.7	
	*MCV	74.3	fL	59.0 - 76.0	
	*MCH	25.3	pg	21.9 - 26.1	
	*MCHC	34.0	g/dL	32.6 - 39.2	
	*Reticulocytes	83.3	10^9/L	<=110.0	
	*Reticulocyte Haemoglobin	26.1	pg	24.5 - 31.8	
	*WBC	10.1	10^9/L	4.9 - 17.6	
	*% Neutrophils	69.8	%		
	*% Lymphocytes	20.4	%		
	*% Monocytes	6.5	%		
	*% Eosinophils	3.1	%		
	*% Basophils	0.2	%		
	*Neutrophils	7.05	10^9/L	2.94 - 12.67	
	*Lymphocytes	2.06	10^9/L	1.06 - 4.95	
	*Monocytes	0.66	10^9/L	0.13 - 1.15	
	*Eosinophils	0.31	10^9/L	0.07 - 1.49	
	*Basophils	0.02	10^9/L	0.00 - 0.10	
	*Platelets	218	10^9/L	143 - 448	

Investigations

Glucose	**3.65**	4.11 - 7.95 mmol/L
Creatinine	**299**	44 - 159 µmol/L
Urea	**29.7**	2.5 - 9.6 mmol/L
BUN: Creatinine Ratio	25	
Phosphorus	**3.75**	0.81 - 2.20 mmol/L
Calcium	**3.05**	1.98 - 3.00 mmol/L
Sodium	**140**	144 - 160 mmol/L
Potassium	**8.1**	3.5 - 5.8 mmol/L
Na: K Ratio	17	
Chloride	**99**	109 - 122 mmol/L
Total Protein	68	52 - 82 g/L
Albumin	29	23 - 40 g/L
Globulin	40	25 - 45 g/L

How do you manage an Addisonian crisis in the short term?

Acute Management

+ IVFT is mainstay of treatment
+ Glucose +/- insulin +/- calcium gluconate may be required for management of hyperkalaemia
+ ACTH stim for definitive diagnosis
+ Dexamethasone will not cross react with cortisol assay for ACTH stim at lab

How do you manage a hyponatremic and/or hyperkalemic hypoadrenocorticism patient in the longer term?

Zycortal® use

- Zycortal® Data sheet starting dose is 2.2mg/kg every 25days
- Studies show that lower doses are sufficient for most dogs
  - Tend to start at 1.5mg/kg every 28days if >1year age
  - Start at 2.2mg/kg every 28days if <1 year age
- Generally, give 0.5mg/kg prednisolone while in hospital then taper at home. Final dose usually around 0.05-0.1mg/kg SID.

Sieber-Ruckstuhl NS, Reusch CE, Hofer-Inteeworn N, Kuemmerle-Fraune C, Müller C, Hofmann-Lehmann R, Boretti FS. Evaluation of a low-dose desoxycorticosterone pivalate treatment protocol for long-term management of dogs with primary hypoadrenocorticism. J Vet Intern Med. 2019 May;33(3):1266-1271. doi: 10.1111/jvim.15475.

When should I recheck electrolytes?
Do I need to worry about Na:K ratio?

Electrolyte monitoring

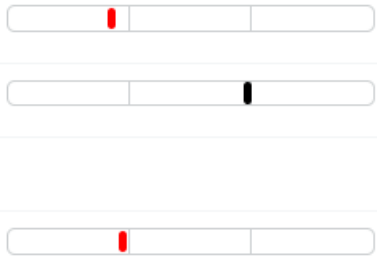
- Na:K ratio can be confusing and problematic
- Repeat electrolytes at day 10 and day 28
- Aim to keep potassium and sodium within their reference ranges (RRs) throughout the dosing interval
- Monitoring electrolytes at day 10 enables assessment of the peak effect of the dose
- Monitoring electrolytes at day 28 enables assessment of the duration of the dose

What happens if electrolytes are abnormal at day 10 and day 28?

Electrolyte abnormalities at day 10 and day 28

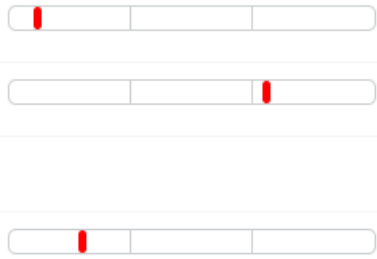
+ Day 10 electrolytes

Sodium	**141**	144 - 160 mmol/L
Potassium	5.8	3.5 - 5.8 mmol/L
Na: K Ratio	24	
Chloride	**108**	109 - 122 mmol/L



+ Day 28 electrolytes

Sodium	**121**	144 - 160 mmol/L
Potassium	**6.1**	3.5 - 5.8 mmol/L
Na: K Ratio	20	
Chloride	**88**	109 - 122 mmol/L



Dose changes

- These results suggest that the duration and/or dose of zycortal was inadequate
- It is easier to change the dose than the duration
- As there was hyponatraemia at day 10 and there is hyponatraemia and hyperkalaemia at day 28 the dose needs to be increased
- Dose should be increased by 10-20%

Electrolyte abnormalities at day 28

+ Day 10 electrolytes

Sodium	148	144 - 160 mmol/L
Potassium	4.1	3.5 - 5.8 mmol/L
Na: K Ratio	36	

+ Day 28 electrolytes

Sodium	155	144 - 160 mmol/L
Potassium	**3.2**	3.5 - 5.8 mmol/L
Na: K Ratio	39	

Dose changes

- These results suggest that the duration and/or dose of Zycortal was too high
- As there was hypokalaemia at day 28 no zycortal should be given until electrolytes are within normal limits
- Dose should then be decreased by 10-20%

Can I monitor response to treatment using the ACTH stimulation test?

Monitoring

+ No, the ACTH stimulation test will remain flatline

+ Need to monitor based on clinical signs and electrolyte values

How do I diagnose a eunatraemic, eukalaemic hypoadrenocorticism patient?

ACTH Stimulation test

ENDOCRINOLOGY

ALERT	TEST	RESULT	UNITS	REF.INTERVAL
Low	Cortisol - Baseline	<10.0	nmol/L	25.0 - 125.0
Low	Cortisol - Post ACTH	<10.0	nmol/L	125.0 - 520.0

Aldosterone stimulation test

ENDOCRINOLOGY

ALERT	TEST	RESULT	UNITS	REF.INTERVAL
Low	Cortisol - Baseline	<10.0	nmol/L	25.0 - 125.0
Low	Cortisol - Post ACTH	<10.0	nmol/L	125.0 - 520.0
	*Aldosterone (#)	217	pmol/L	0 - 393
	*Aldosterone - Post ACTH (#)	439	pmol/L	82 - 859

What treatment would you give for an “atypical” patient?

Treatment

Prednisolone 0.05-0.2mg/kg SID

No need for DOCP at this stage but will need to monitor electrolytes

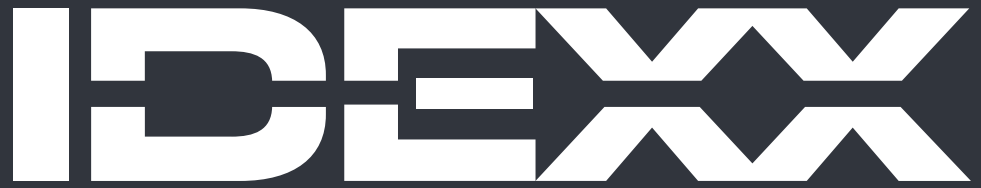
If aldosterone was low then either closely monitor or consider low dose DOCP

Ettinger's Textbook Of Veterinary Internal Medicine. 9th Edition, Volume 2. Chapter 296, Hypoadrenocorticism. P 2042

Summary

1. ACTH stimulation is the diagnostic test of choice
2. ACTH stimulation test is not suitable for monitoring
3. If no evidence of aldosterone deficiency, then only prednisolone therapy is needed
4. Adjust Zycortal dose according to sodium and potassium values at day 10 and day 28 and not the NA/K ratio

Questions?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