CREATING CLARITY

Taking the stress out of diagnosing and monitoring adrenal disease

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IDEXX

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Conflicts of Interest & Disclaimer

Ana Jacinto

+ Part-time employee of IDEXX Laboratories UK
+ Part-time employee of IVC Evidensia Portugal

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 exam and presentation, and laboratory data. With respect to any drug therapy or monitoring program, you should refer to applicable product insert(s) for complete description of dosage, indications, interactions, and cautions. Diagnosis, treatment, and monitoring should be patient specific and is the responsibility of the veterinarian providing primary care.

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Agenda

Objective

1. The adrenal gland
2. Cushing's syndrome
3. Diagnostic approach
4. Endocrine tests
5. Monitoring treatment
6. *Hypoadrenocorticism*
7. *Diagnostic approach*
8. *Monitoring Treatment*

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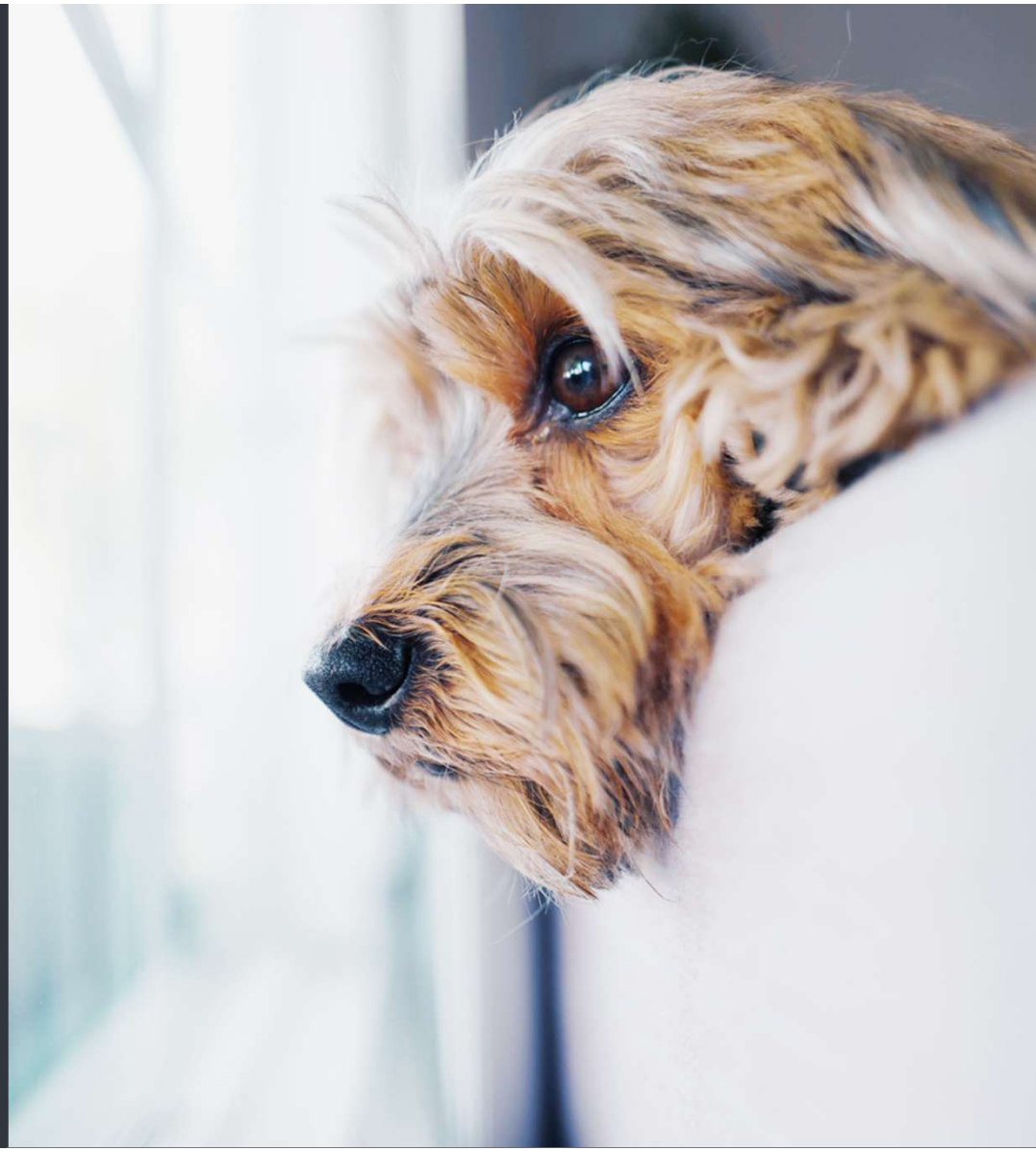
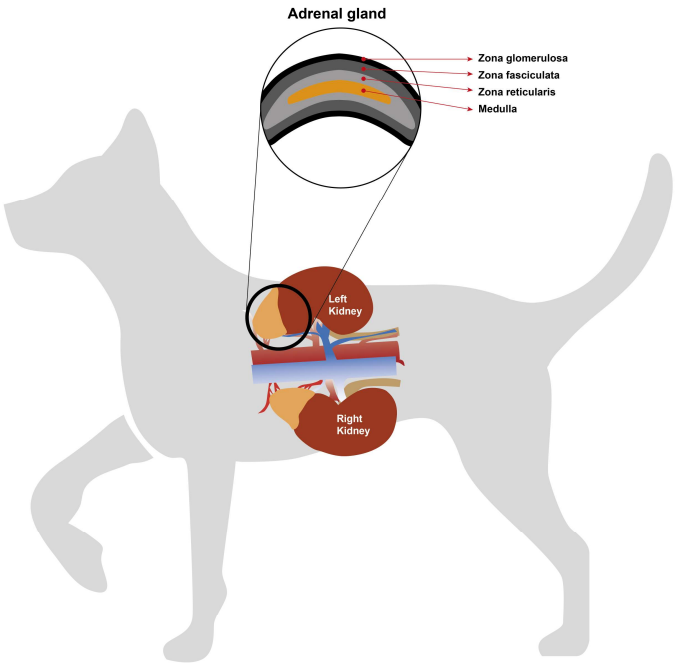
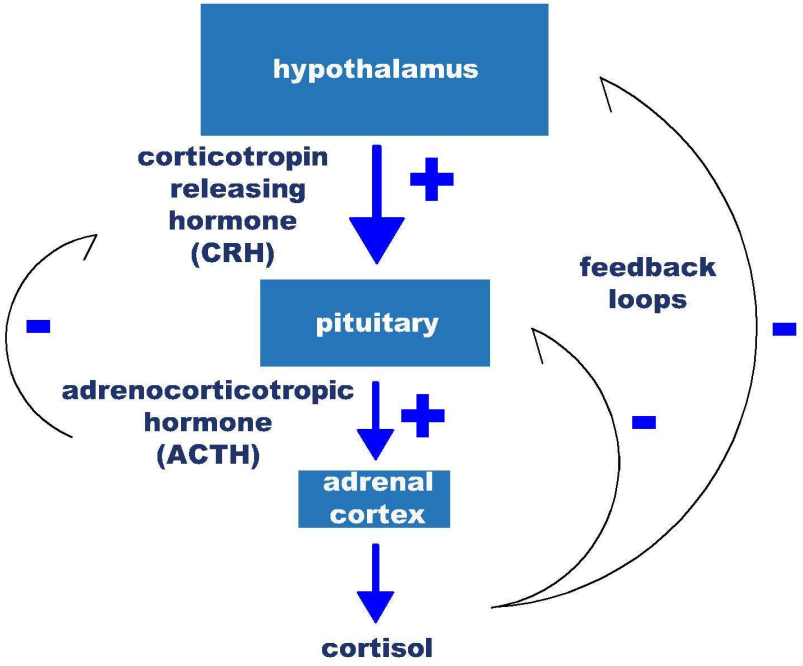
Adrenal Gland



The adrenal gland and the hypothalamic-pituitary-adrenal axis





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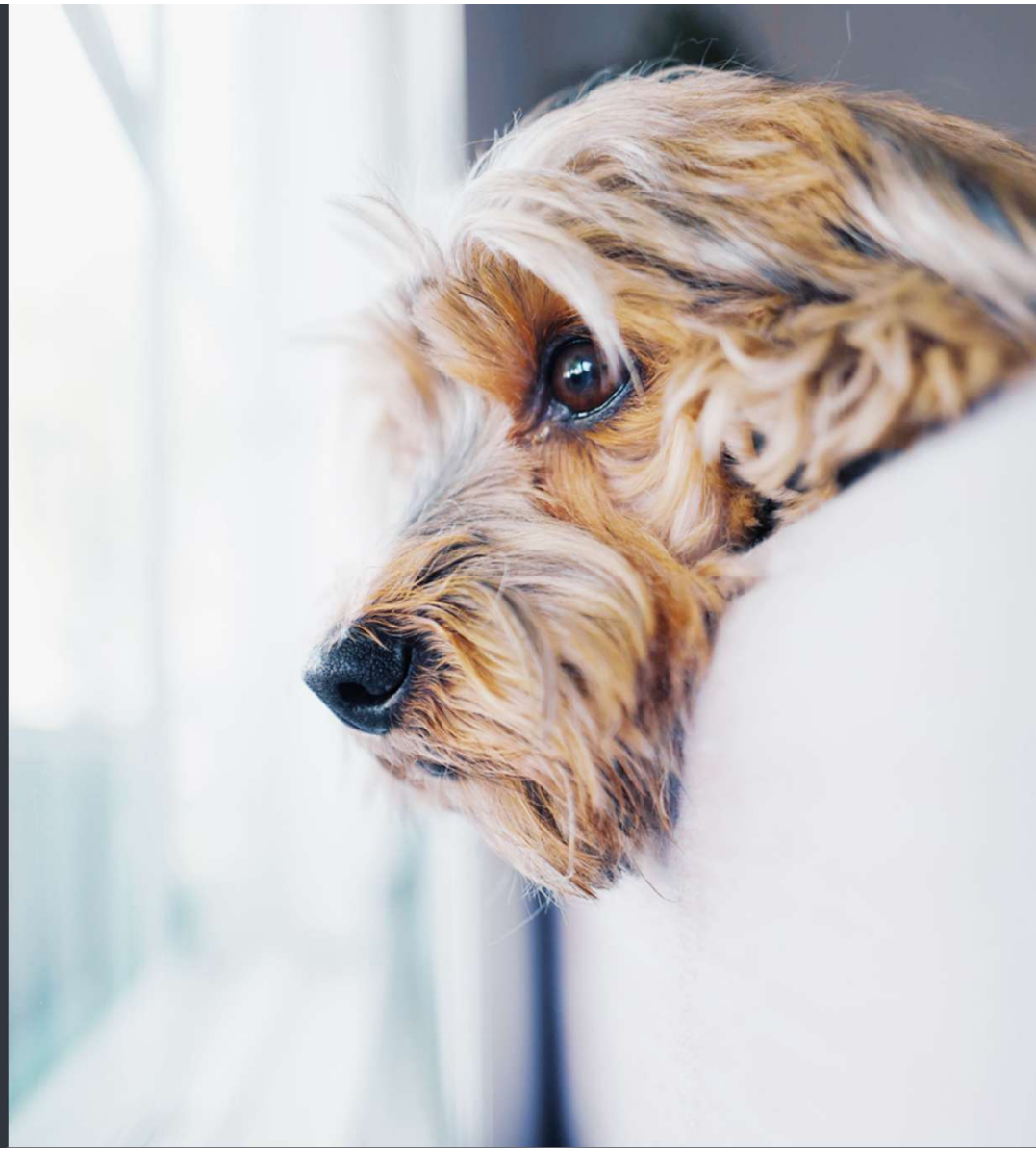
Cushing’s Syndrome



Cushing’s Syndrome

Clinical syndromes caused by chronic excessive glucocorticoid activity, due to endogenous or exogenous steroid hormones.

Hypercortisolism (previously hyperadrenocorticism)

Elevated cortisol leading to increased glucocorticoid activity.

Photo Ana Jacinto

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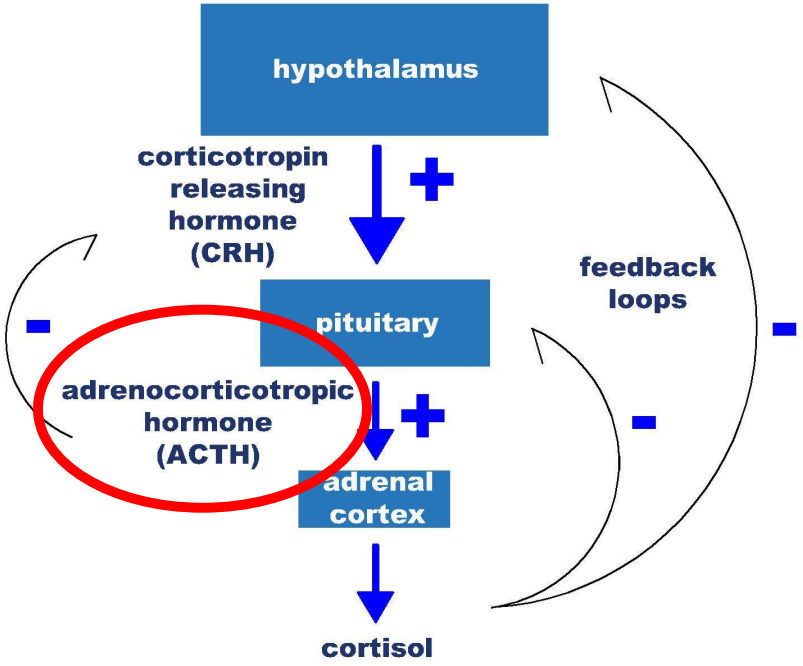
Naturally-occurring Cushing's Syndrome

ACTH-dependent

Pituitary-dependent
+ Pituitary neoplasia
+ Pituitary hyperplasia

Ectopic ACTH secretion
+ *Carcinoid*

Subdiagnostic Cushing's Syndrome



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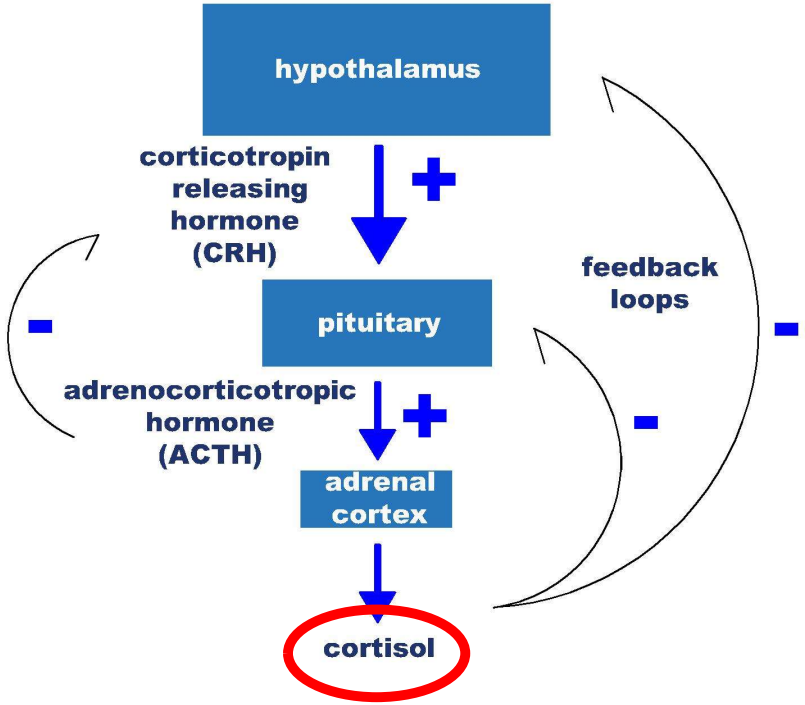
Naturally-occurring Cushing's Syndrome

ACTH-independent

Adrenal dependent hypercortisolism
+ Adrenal neoplasia
+ Adrenal hyperplasia

Aberrant adrenal receptor expression
Subdiagnostic Cushing's Syndrome



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Iatrogenic Cushing's Syndrome

- Exogeneous glucocorticoid or progestins therapy
- Clinical signs resolve after withdrawing glucocorticoids
- Most common cause of Cushing's Syndrome!

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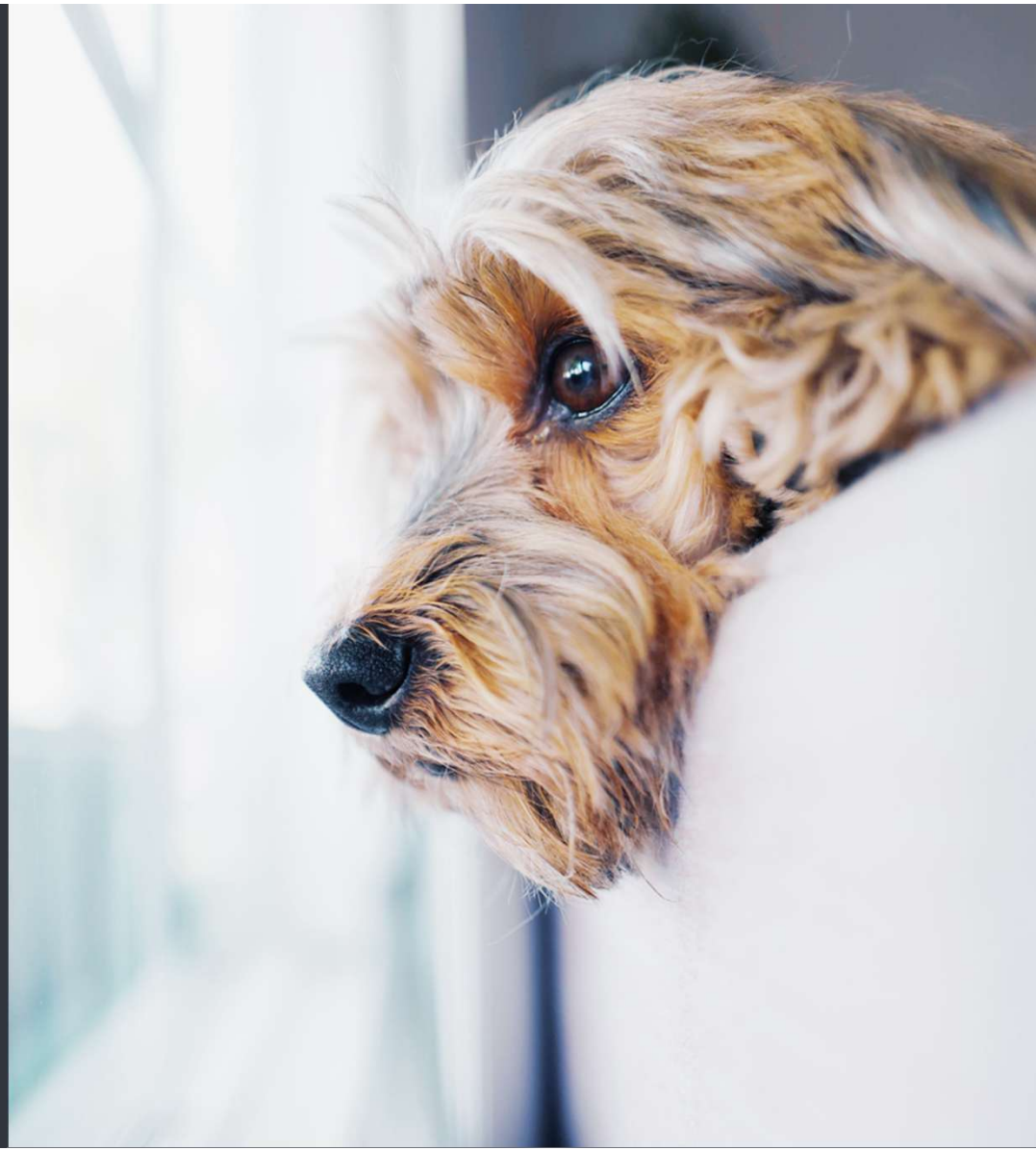
Diagnostic Approach



Signalment

Image Ana Jacinto

- 9-year-old
- Male-neutered
- Miniature Poodle

- Middle-aged to older dogs
  - majority >9y old
- Poodles, Dachshund, Terrier breeds…
- Female > Male

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History and Physical Examination

Image Ana Jacinto

+ Less active
+ Polyuria / Polydipsia
+ Polyphagia
+ Hypotrichosis, alopecic areas
+ Pot bellied appearance

+ ≈ 90% Polyuria / Polydipsia
+ Polyphagia
+ Panting
+ Pendulous abdomen
+ Endocrine alopecia

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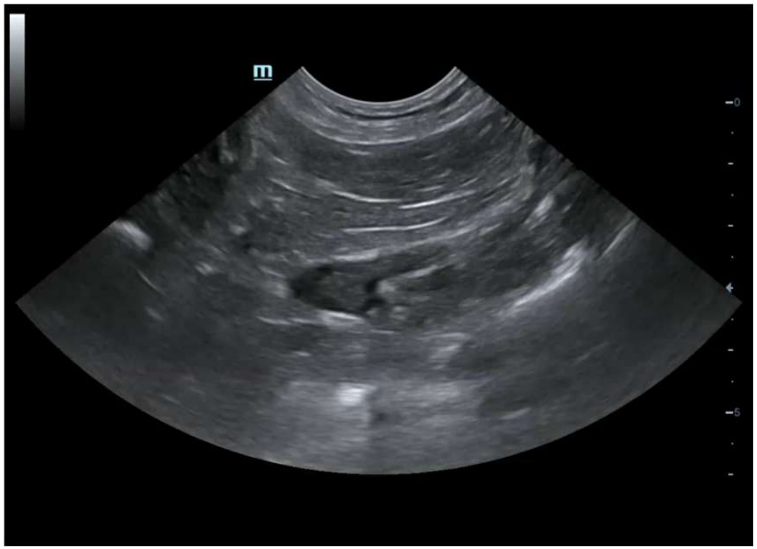
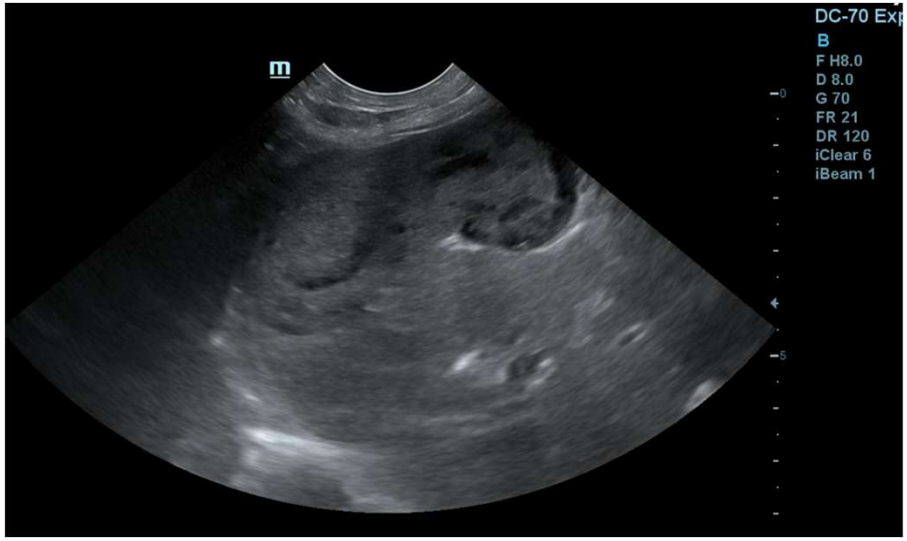
Other Findings…





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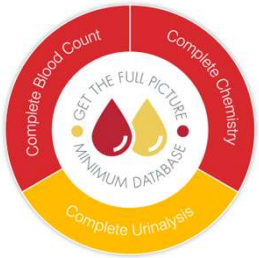
Haematology

RBC		8.88	5.39 - 8.70 x10^12/L	
Haematocrit		0.609	0.383 - 0.565 L/L	
Haemoglobin		219	134 - 207 g/L	
MCV		68.6	59.0 - 76.0 fL	
MCH		24.7	21.9 - 26.1 pg	
MCHC		360	326 - 392 g/L	
Reticulocytes	a	111.9	<= 110.0 K/µL	
Neutrophils		13.38	2.94 - 12.67 x10^9/L	
Lymphocytes		1.03	1.06 - 4.95 x10^9/L	
Monocytes		1.28	0.13 - 1.15 x10^9/L	
Eosinophils		0.09	0.07 - 1.49 x10^9/L	
Basophils		0.02	0.00 - 0.10 x10^9/L	
Platelets		562	143 - 448 x10^9/L	
Blood Film Evaluation		No morphological abnormalities detected in red blood cells. No abnormal white cells seen.		



+ Stress leukogram
+ Lymphopaenia
+ Thrombocytosis
+ Erythrocytosis

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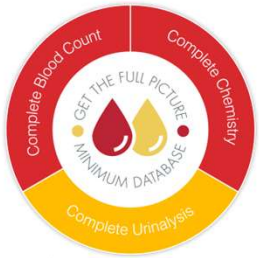
Serum Biochemistry



ALT	85.3	19.8 - 124.0 U/L	
ALP	416.0	0.0 - 130.0 U/L	
GGT	26.9	2.0 - 5.7 U/L	
Cholesterol	10.97	3.20 - 6.20 mmol/L	

- Increased ALP (often marked)
- Increased ALT (mild to moderate)
- Mild to moderately increased cholesterol and triglyceride
- Mild fasting hyperglycaemia
- Decreased urea
- Bile acids mildly raised
- cPLI may be increased without clinical pancreatitis

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Urinalysis

	Collection Method	Free Catch
	Colour	Pale Yellow
	Clarity	Clear
	Specific Gravity	1.022
	pH	5.0
	Urine Protein	3+
	Glucose	neg

	Urine Creatinine	12,464.4	µmol/L
	Urine Protein	3.47	g/L
	Urine Protein: Creatinine Ratio	2.47	

- USG <1.020 in most cases (often <1.012)
- UPC >0.5 in most cases (but usually not higher than 6)
- Bacteriuria

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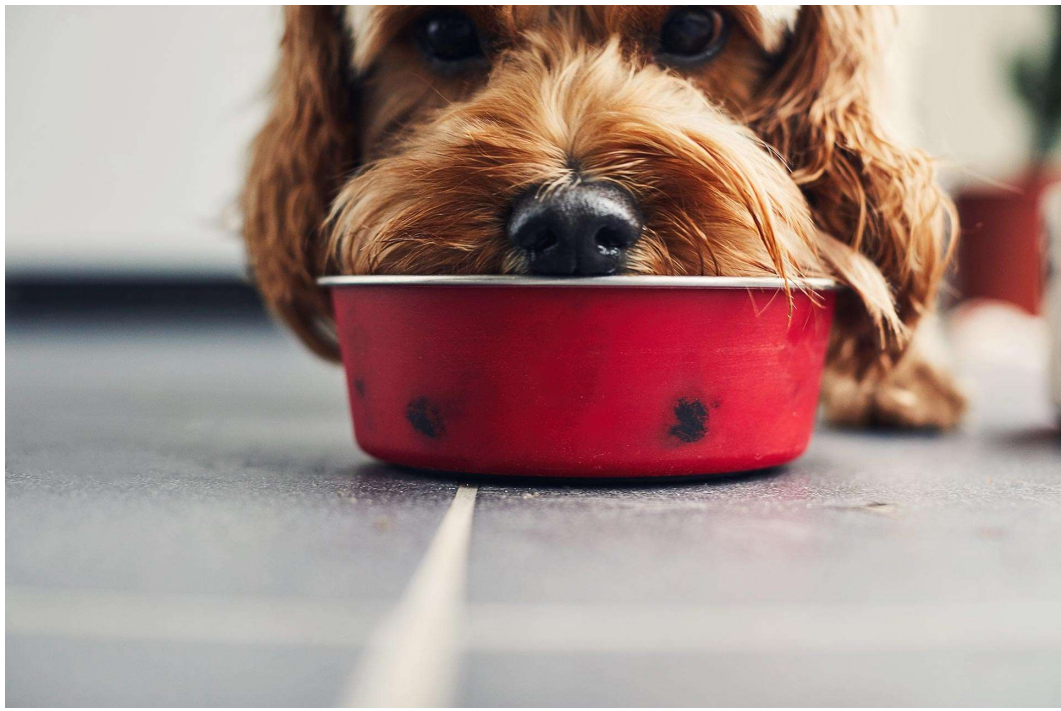
Endocrine Tests

When to test for Cushing's Syndrome?

1. Suggestive clinical signs
2. Supportive clinical pathological findings
3. USG typically <1.020



IDEXX Stock

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Endocrine Tests

+ When not to test for Cushing's Syndrome?

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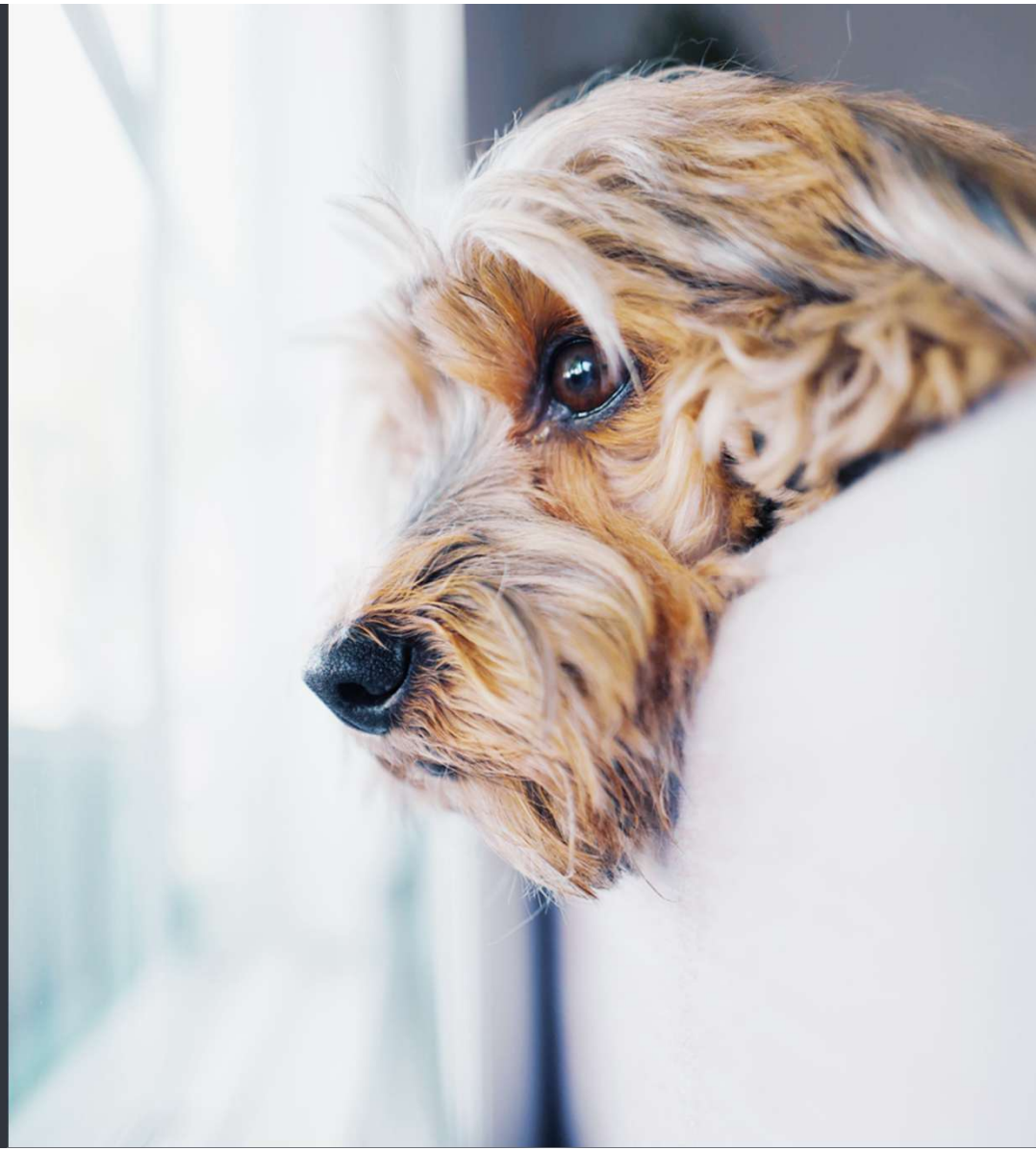
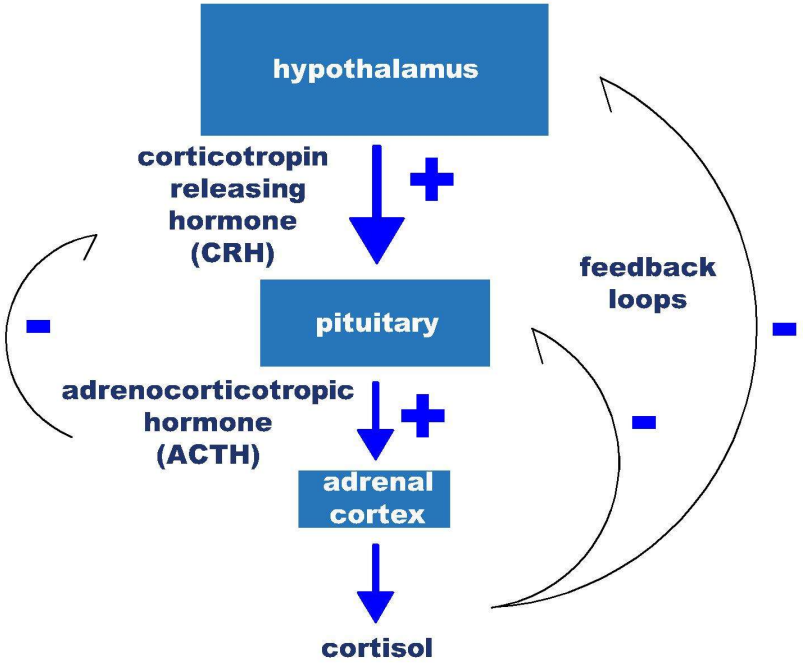
Endocrine Tests



Endocrine Tests

Diagnosis of hypercortisolism

+ Increase in cortisol production
+ Decreased sensitivity to negative glucocorticoid feedback



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Cortisol

In https://www.idexx.com/en/veterinary/analyzers/catalyst-one-chemistry-analyzer/test-menu/cortisol/ Accessed May 2026

+ Canine Catalyst Cortisol
+ Quantitative immunoassay
+ Whole blood (Catalyst lithium heparin whole blood separator), serum, and lithium heparin plasma
+ Avoid icteric or moderately to severely haemolyzed samples
+ Prednisolone cross reacts with assay
+ Corticosteroids alter pituitary-adrenal function

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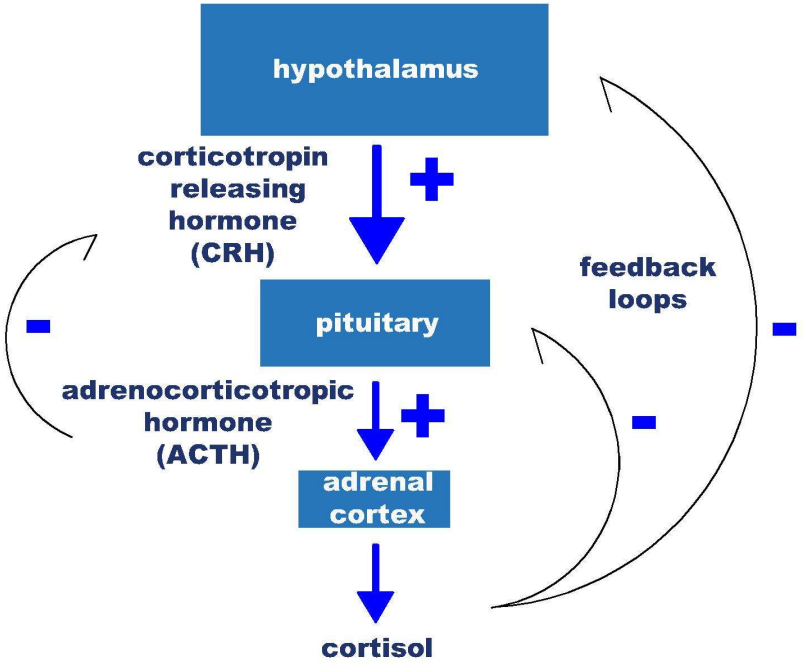
Endocrine Tests

Diagnosis of hypercortisolism

+ Increase in cortisol production
+ Decreased sensitivity to negative glucocorticoid feedback

+ Some medications may impact results



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STANDARD ARTICLE

Journal of Veterinary Internal Medicine ACVIM Open Access American College of Veterinary Internal Medicine

The impact of single-dose trazodone administration on plasma endogenous adrenocorticotropic hormone and serum cortisol concentrations in healthy dogs

Morgan Brown[1] | Tekla Lee-Fowler[1] | Ellen N. Behrend[1] | Megan Grobman[1,2]

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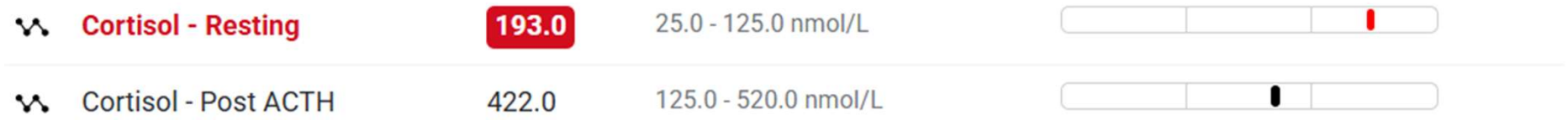
Basal Cortisol

+ Fluctuates widely
+ Not useful for Cushing's syndrome diagnosis
+ Resting cortisol >55 nmol/l makes hypoadrenocorticism unlikely



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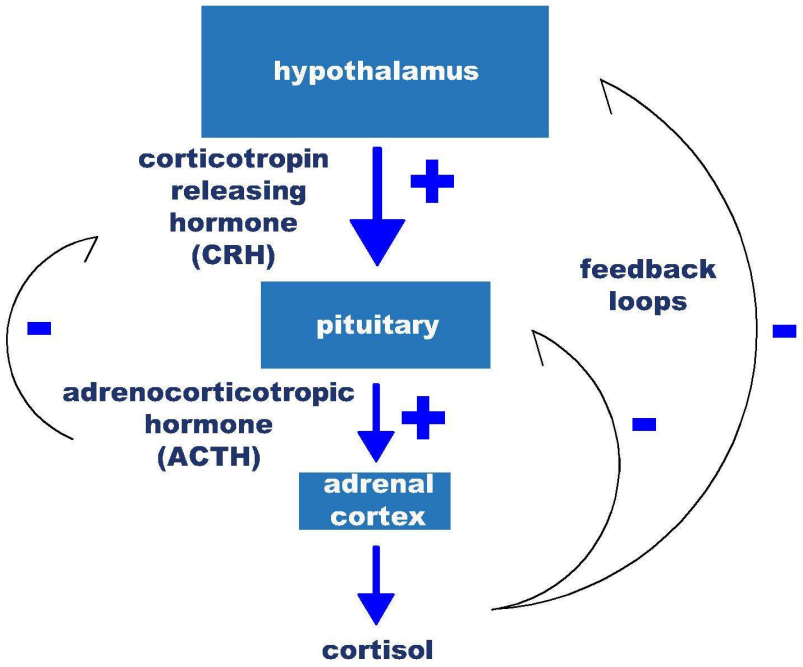
Endocrine Screening Tests

+ **Urine cortisol:creatinine ratio**
- Indicative of glucocorticoid secretion over several hours
- Single urine sample sufficient

+ **ACTH stimulation test**
- Response to maximal ACTH stimulation
- Diagnosis of Cushing's syndrome and hypoadrenocorticism
- Differentiation between iatrogenic and spontaneous HAC

+ **Low dose dexamethasone suppression test**
- Assesses pituitary adrenal axis feedback pathway



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Urine Cortisol: Creatinine Ratio

+ High sensitivity
+ But….Very low specificity …
+ Increased with many conditions
+ Collection of sample at least 2d after visiting vet

	Urine Cortisol: Creatinine Ratio	a	326.4	x10-6
	Cortisol - Resting		77.5	nmol/L
	Cortisol - 4 hr Post Dex		<13.8	nmol/L
	Cortisol - 8 hr Post Dex		<13.8	nmol/L

Photo Ana Jacinto

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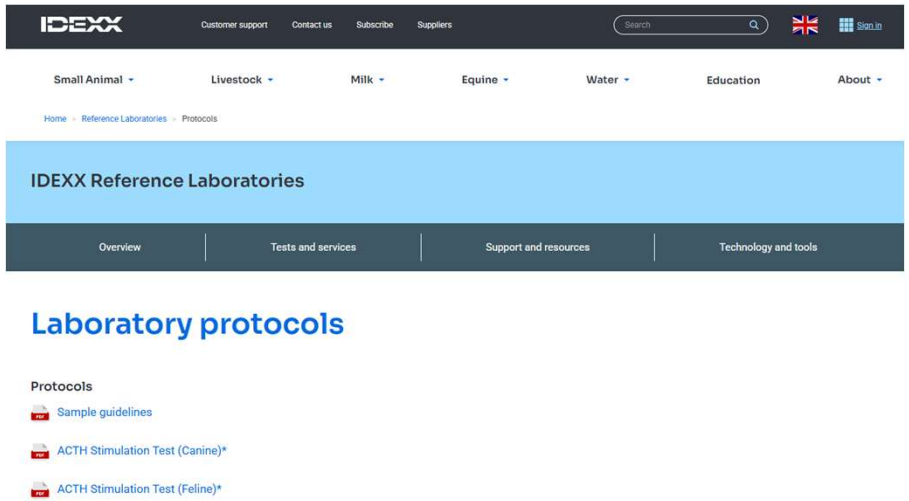
Test Protocols



Laboratory protocols

Protocols

- Sample guidelines
- ACTH Stimulation Test (Canine)*
- ACTH Stimulation Test (Feline)*

IDEXX

Canine ACTH stimulation test

Indications

- Diagnosis of hyperadrenocorticism (Cushing's syndrome)
- Diagnosis of hypoadrenocorticism (Addison's syndrome) or iatrogenic hyperadrenocorticism
- Monitoring of adrenal reserve in patients receiving trilostane (or occasionally mitotane) treatment for hyperadrenocorticism.

Notes

- The ACTH stimulation test has a lower sensitivity but higher specificity than the low-dose dexamethasone suppression test (LDDST) for the diagnosis of canine hyperadrenocorticism.
- The results of the ACTH stimulation can be affected by prior glucocorticoid administration (including topical medications), stress (excitement) and other/concurrent disease.

IDEXX

Low-Dose Dexamethasone Suppression Test (Canine)

Indications

- Screening test for naturally occurring hyperadrenocorticism (Cushing's syndrome).
- Not indicated for monitoring patients receiving trilostane therapy.
- Cannot be used for the diagnosis of hypoadrenocorticism (Addison's disease).

Notes

- Avoid patient stress or concurrent diagnostic procedures for the duration of the low-dose dexamethasone suppression (LDDS) test (8h).
- The reported sensitivity for the LDDS test for diagnosis of hyperadrenocorticism is ≈95%, suggesting it is more sensitive than the ACTH stimulation test for this purpose.

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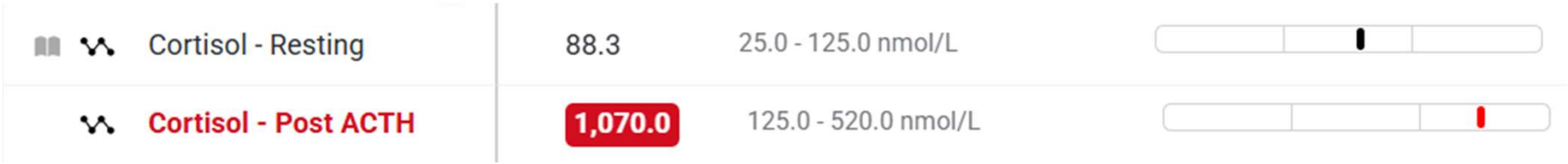
ACTH Stimulation Test

- Collect basal blood sample
- Inject at least 5 µg/kg of ACTH (tetracosactide)* intravenously
    - IM can be considered if IV not possible
- Obtain 2nd sample 1hr later
- Measure cortisol on both samples

**Allerton, F. (Ed.) (2023). BSAVA Small Animal Formulary, Part A: Canine and Feline (11th ed.). British Small Animal Veterinary Association*



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ACTH Stimulation Test

+ Evaluates adrenocortical response to maximal ACTH stimulation

+ Exaggerated response in naturally occurring HAC
+ Sub-normal response in iatrogenic HAC
+ Measurement of 17-hydroxyprogesterone?

+ Sensitivity ADH around 60%
+ Sensitivity PDH around 85%
+ Specificity around 85%

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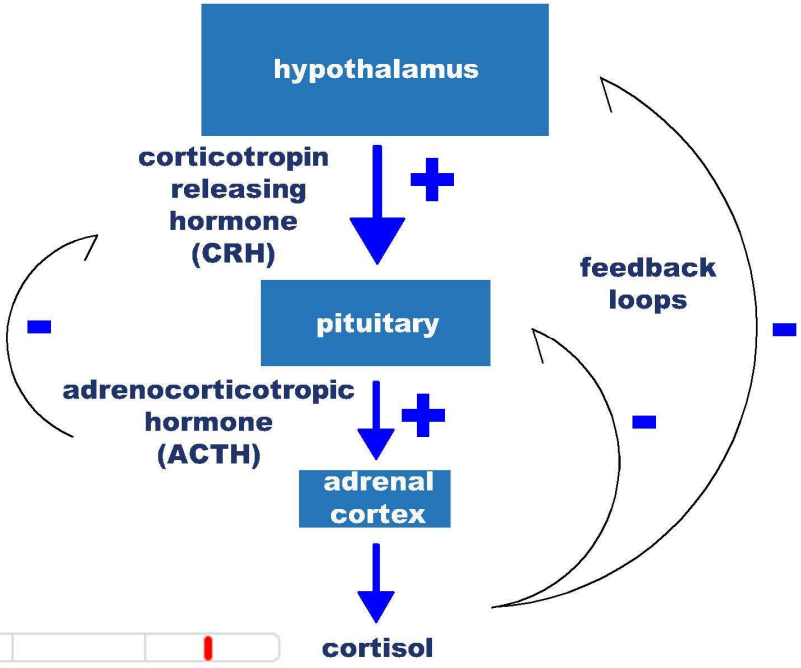
Low Dose Dexamethasone Suppression Test

- Baseline blood sample
- Inject 0.01 – 0.015 mg/kg of dexamethasone intravenously
- Obtain 2nd sample 4hr later
- Obtain 3rd sample 8hr later
- Measure cortisol on all samples



Cortisol - Resting	281.0	25.0 - 125.0 nmol/L		
Cortisol - 4 hr Post Dex	17.6	nmol/L		
Cortisol - 8 hr Post Dex	24.9	<= 40.0 nmol/L		

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Low Dose Dexamethasone Suppression Test

Cortisol - Resting	110.0	25.0 - 125.0 nmol/L	
Cortisol - 4 hr Post Dex	101.0	nmol/L	
Cortisol - 8 hr Post Dex	**103.0**	<= 40.0 nmol/L	

8h post dexamethasone is consistent with HAC if supportive clinical signs and clin path findings

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What is the Best Test to Confirm Hypercortisolism?

ACTH Stimulation Test

+ Less affected by non adrenal disease
+ Lower sensitivity
+ Does not differentiate b and ADH
+ Differentiates spontaneous from iatrogenic HAC
+ Quick and simple to perform

LDDST

+ Lower specificity
+ Excellent sensitivity
+ confirm PDH
+ useful in iatrogenic HAC
+ Requires 8h to perform

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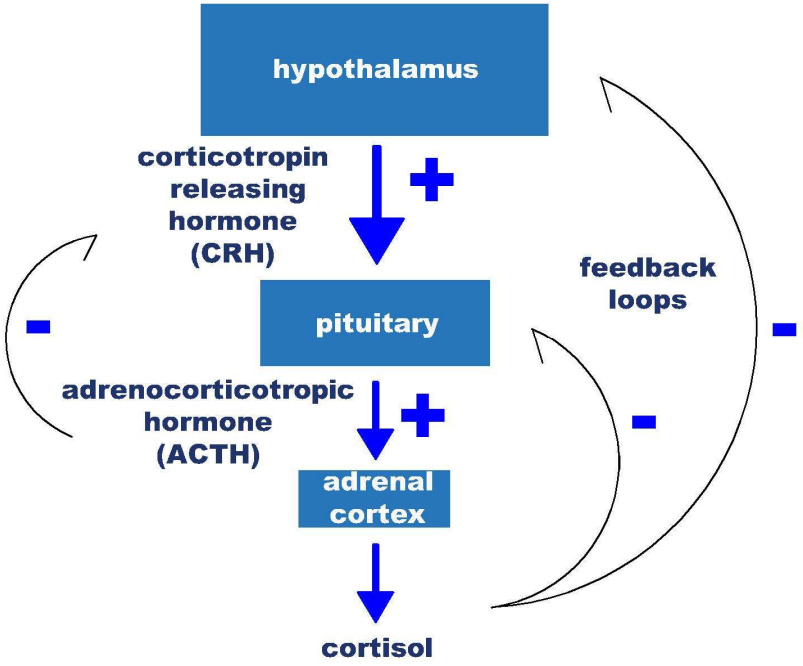
Differentiating Endocrine Tests

+ Low dose dexamethasone suppression test

+ High dose dexamethasone suppression test

+ Endogenous ACTH concentration



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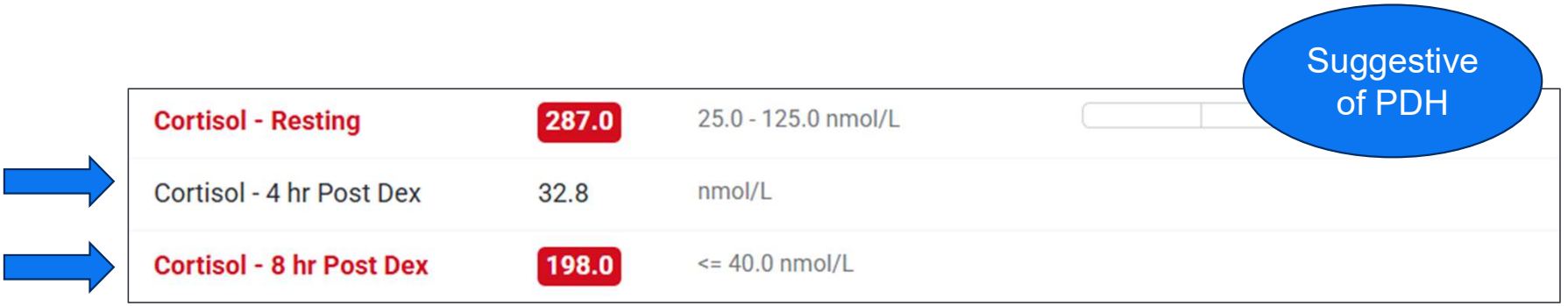
Low Dose Dexamethasone Suppression Test

+ 4-hr cortisol < laboratory cut-off
+ 4-hr cortisol <50% baseline cortisol
+ 8-hr cortisol <50% baseline cortisol and higher than cut-off



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Low Dose Dexamethasone Suppression Test

Cortisol - Resting	110.0	25.0 - 125.0 nmol/L	
Cortisol - 4 hr Post Dex	101.0	nmol/L	
Cortisol - 8 hr Post Dex	**103.0**	<= 40.0 nmol/L	

Useful for diagnosis, but not discriminatory for which type of hypercortisolism

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Differentiating Tests

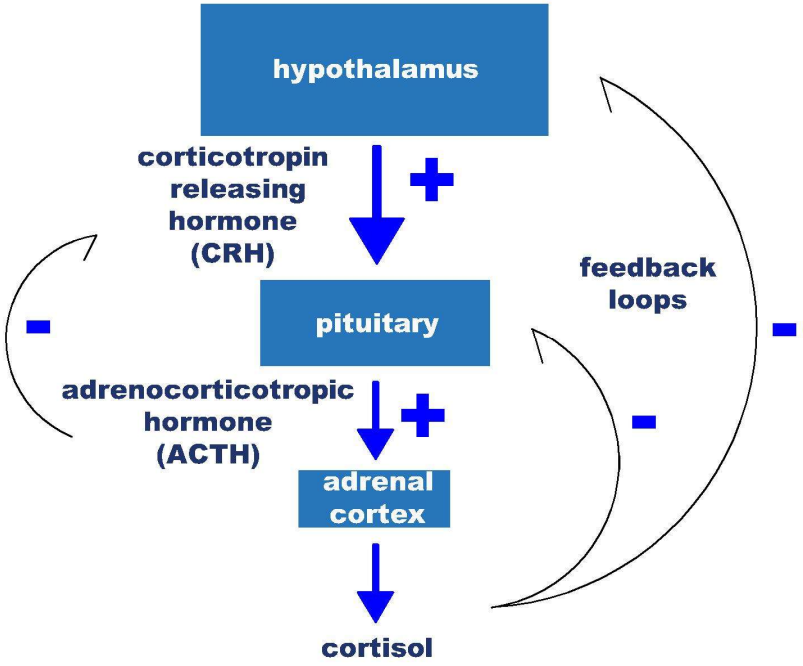
+ High Dose Dexamethasone Suppression Test
+ Dexamethasone 0.1mg/Kg IV

ADH

Lack of suppression

PDH

Only a minority of dogs that show no suppression on the LDDST will show on HDDST



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Differentiating Tests

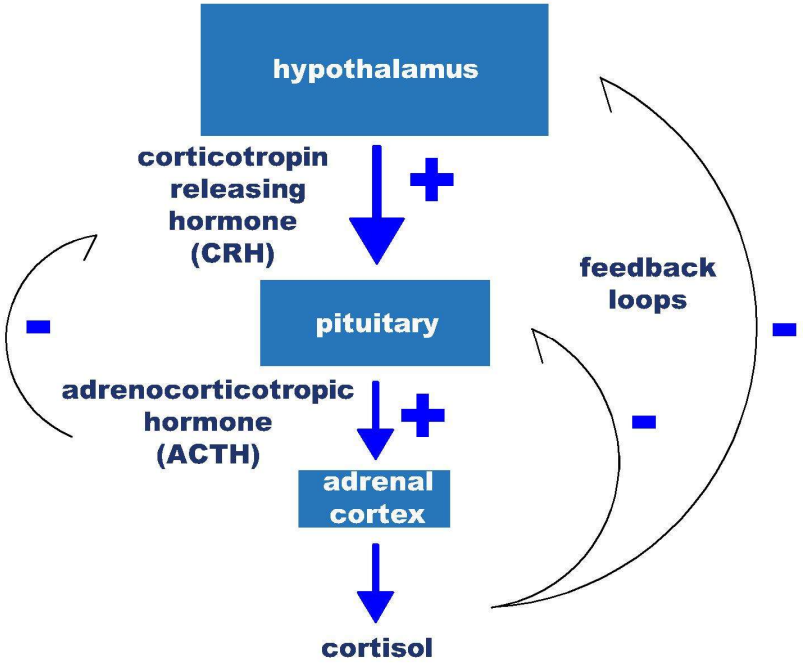
+ Endogeneous ACTH

PDH – *e ACTH* normal to increased

ADH – *e ACTH* low or undetectable

However…. Non diagnostic results can occur

And it is essential to handle the sample properly



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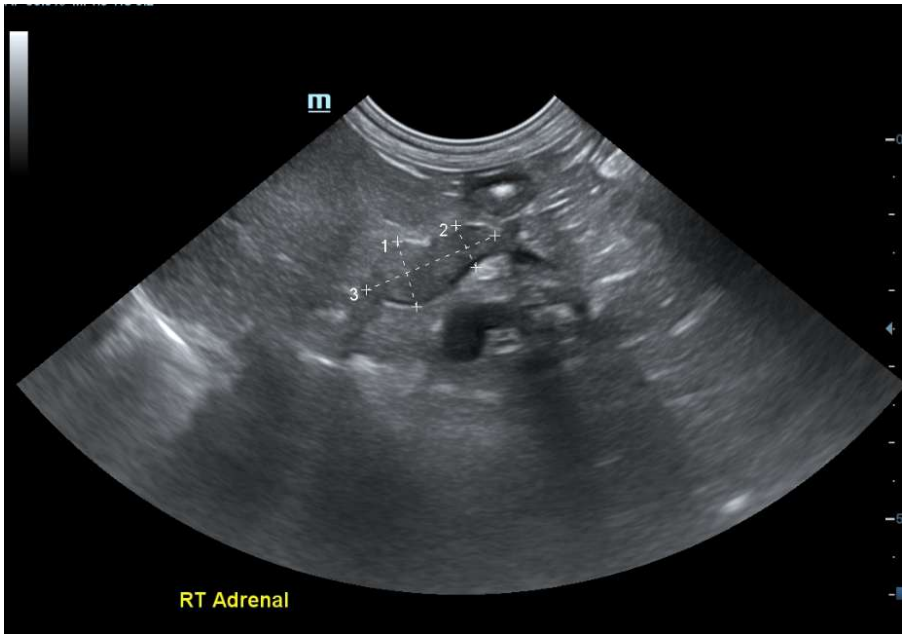
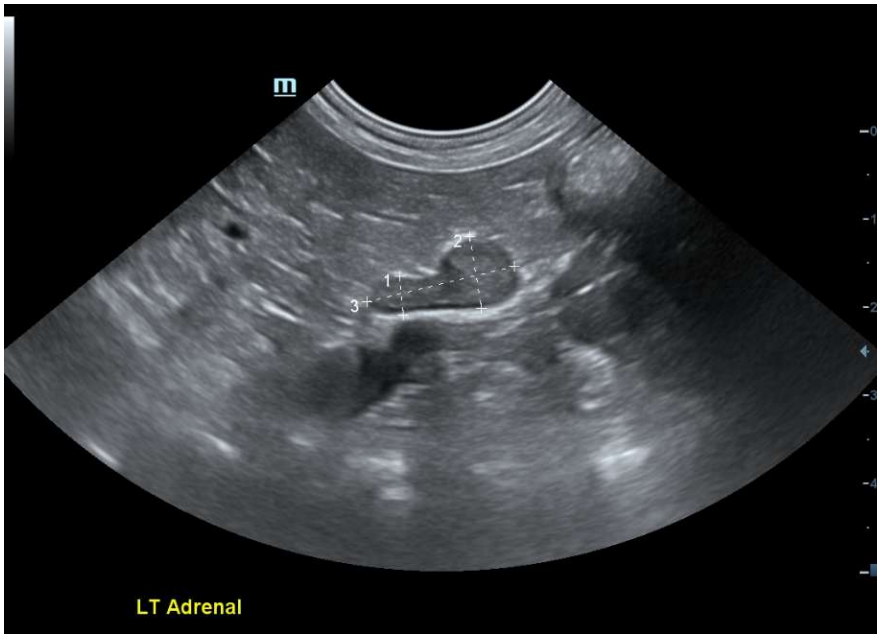
Diagnostic Imaging





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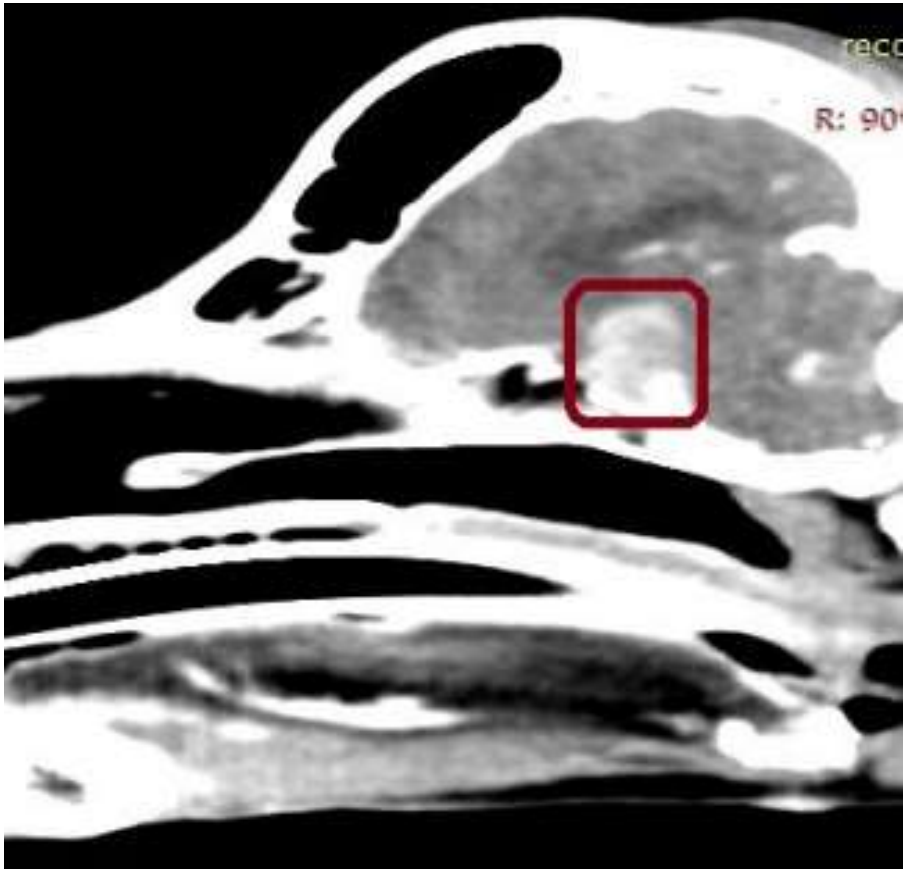
Diagnostic Imaging



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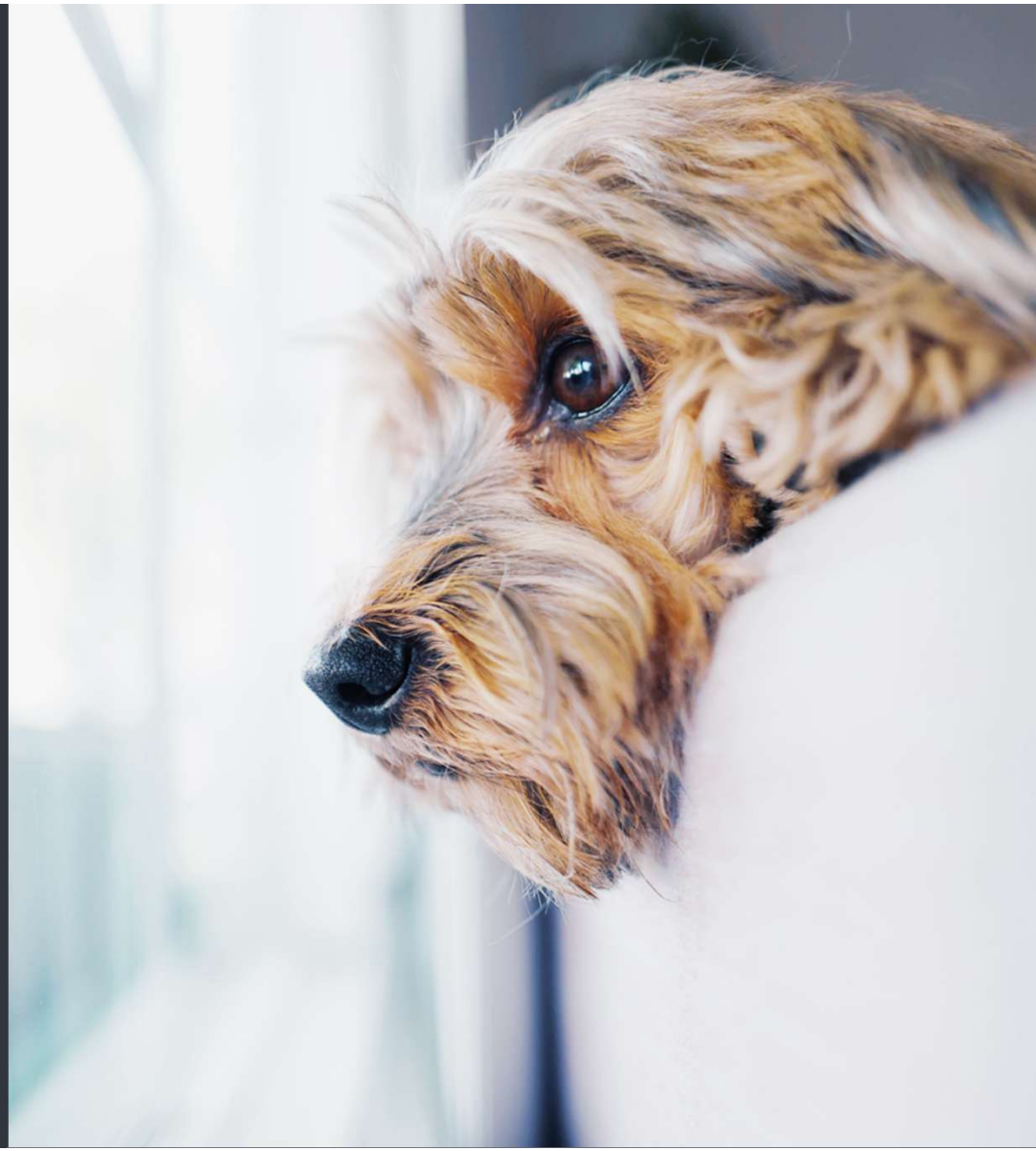
Monitoring Treatment



Trilostane

- Inhibits 3-beta-hydroxysteroid dehydrogenase needed for cortisol and aldosterone synthesis
- Every 12h dosing may result in better control and longer survival
- Possible side effects include transitory hypoadrenocorticism but also adrenal necrosis

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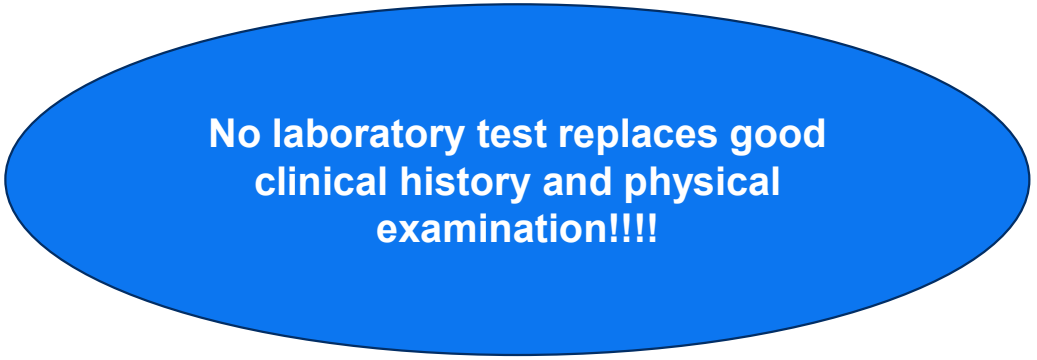
Trilostane

- Monitoring times
  - 10-14d, 30d, 90d, once disease is well controlled every 3 to 6 months
  - 10-14d after any dose adjustment

- Monitoring parameters
  - Clinical Signs
  - Biochemistry panel (including electrolytes)
  - Cortisol testing
  - Endocrine testing
    - ACTH stimulation test
    - Pre-pill cortisol



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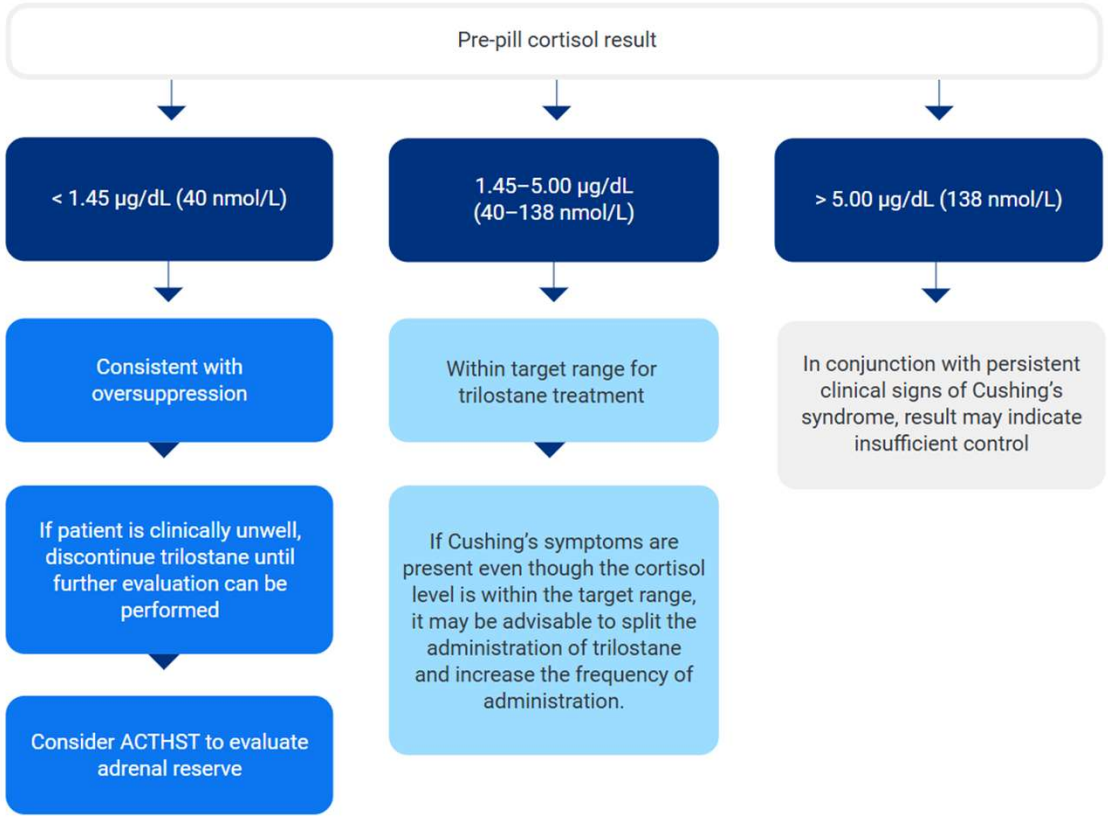
Monitoring with Pre-pill Cortisol



In Clinical Reference Guide Assessed 10.05.2026

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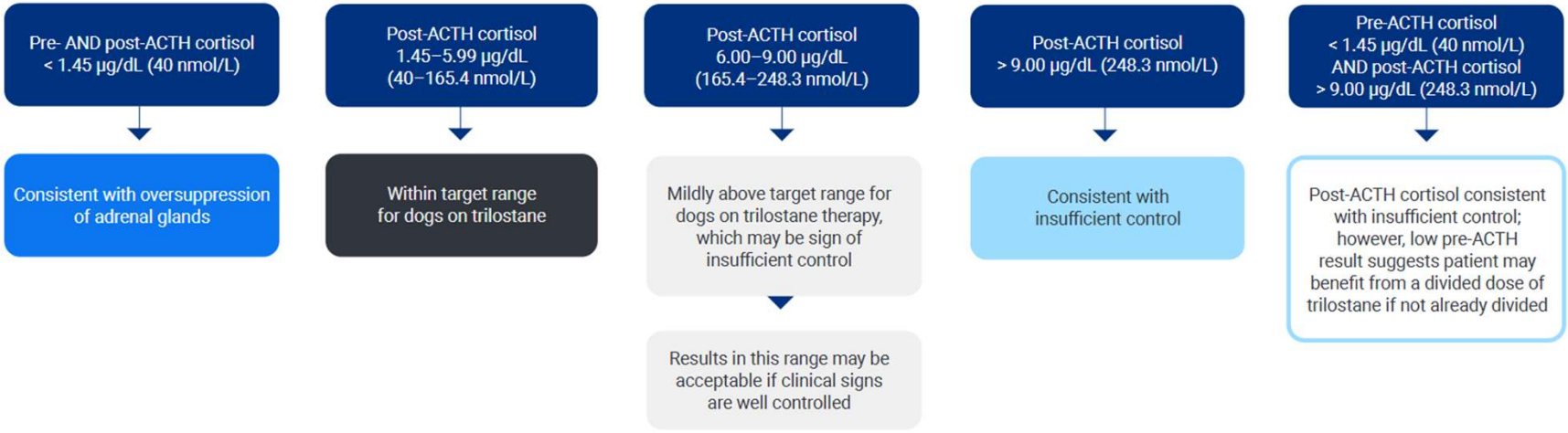
Monitoring with ACTH Stimulation

- Timing of the test should be consistent
- 4-to-6-hour post-pill (*2-3- hour post pill recommended by some veterinary endocrinologists)*
- Clinical decisions depend on clinical signs displayed
- Avoiding overdose is the main aim of the first recheck



In Clinical Reference Guide Assessed 10.05.2026

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ACTH Stimulation Test or Pre-Pill cortisol?

ACTH Stimulation Test

+ Definitive test to diagnose hypoadrenocorticism
+ Direct evaluation of adrenal re
+ Long experience

+ Expensive
+ Has not been always available
+ Time consuming

Pre-Pill Cortisol

+ Simpler
+ In a study had good agreement with owner based scoring scheme

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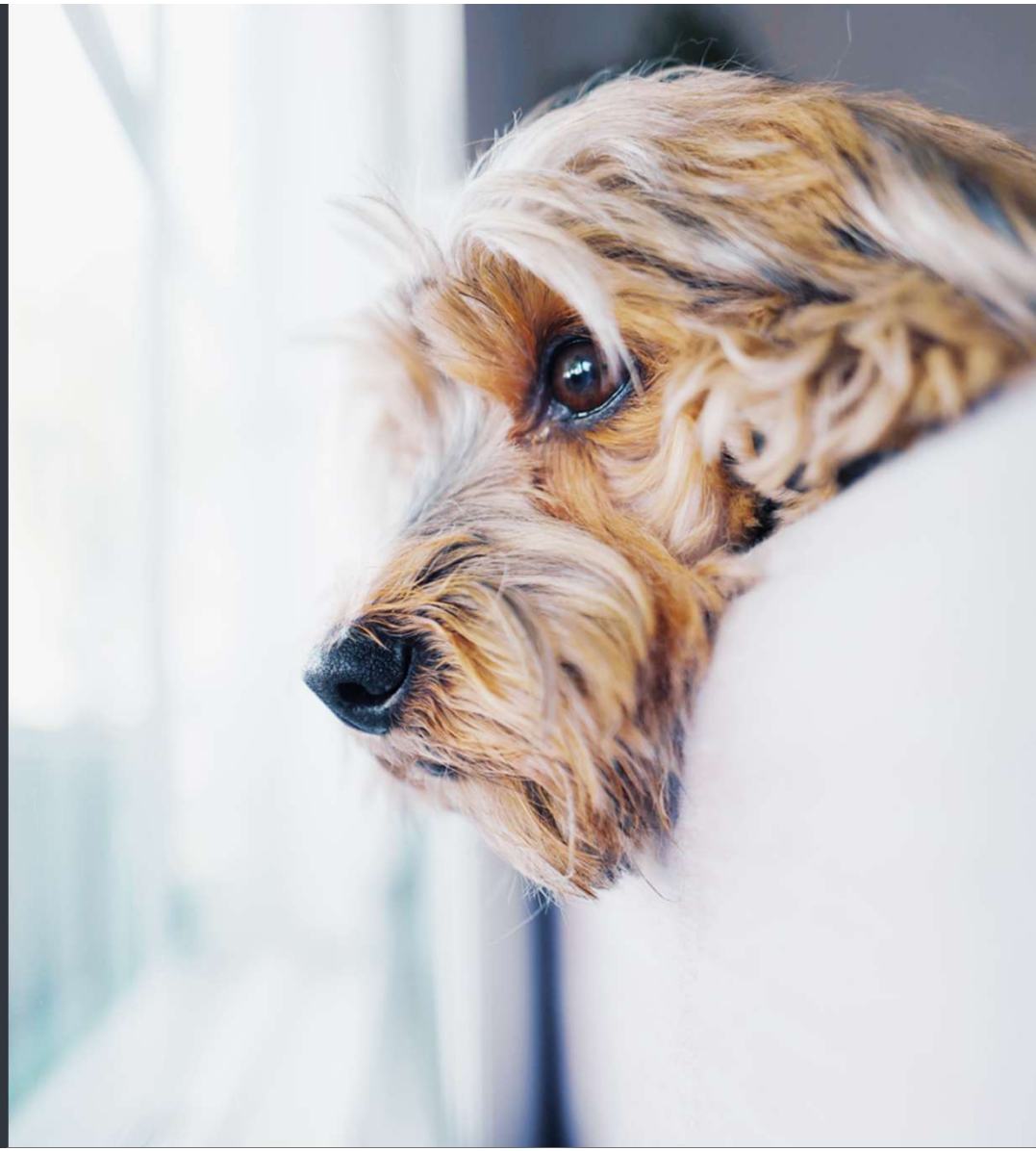
Hypoadrenocorticism



Hypoadrenocorticism

- Reduced adrenal cortex function with consequent state of glucocorticoid deficiency, mineralocorticoid deficiency or both
  - Naturally occurring
  - Iatrogenic
    - Abrupt discontinuation of drugs with glucocorticoid activity
    - Trilostane

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Hyponatremic and/or hyperkalemic hypoadrenocorticism

- Previously typical hypoadrenocorticism
- Primary hypoadrenocorticism
  - AKA Addison's disease

Sodium	142	144 - 160 mmol/L	
Potassium	8.0	3.5 - 5.8 mmol/L	
Na: K Ratio	18		
Chloride	107	109 - 122 mmol/L	

IDEXX Stock

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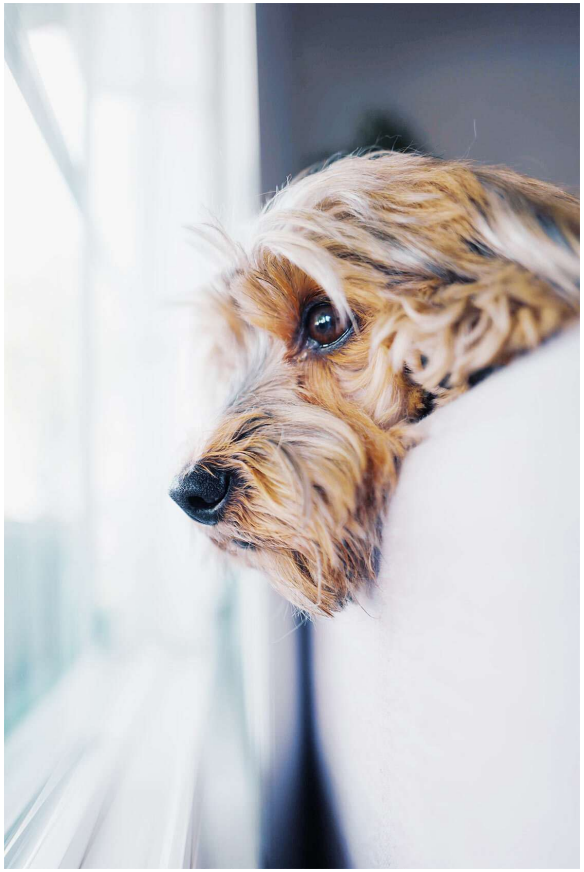
Eunatraemic, eukalaemic hypoadrenocorticism

- Normal electrolytes
- Previously called atypical hypoadrenocorticism
- Primary or secondary hypoadrenocorticism



IDEXX Stock

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When to suspect of hypoadrenocorticism?

Image Ana Jacinto

- 3y old
- Crossbreed, ME

- Anorexia, weight loss
- Lethargy
- Weakness

- Dehydrated 7%
- Abdominal discomfort
- HR 44bpm
- Weak peripheral pulse
- Systolic BP 95mmHg
- Rectal temperature 37.3ºC

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When to suspect of hypoadrenocorticism?

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Not all problems are real!

Phosphorus	0.99	0.81 - 2.20 mmol/L
Calcium	**0.97**	1.98 - 3.00 mmol/L
Sodium	146	144 - 160 mmol/L
Potassium	**9.9**	3.5 - 5.8 mmol/L
Na: K Ratio	15	
Chloride	**108**	109 - 122 mmol/L

LTT-LAVENDER
Top Tube
2 mL or 9 mL
EDTA anticoagulant
lavender cap with white ring

LTT-MINI
Lavender Top Tube
0.5 mL
EDTA anticoagulant
lavender cap

In https://www.idexxbioanalytics.com/hubfs/IBA%20Tube%20Guide%202020%20V12.pdf Accessed May 2026

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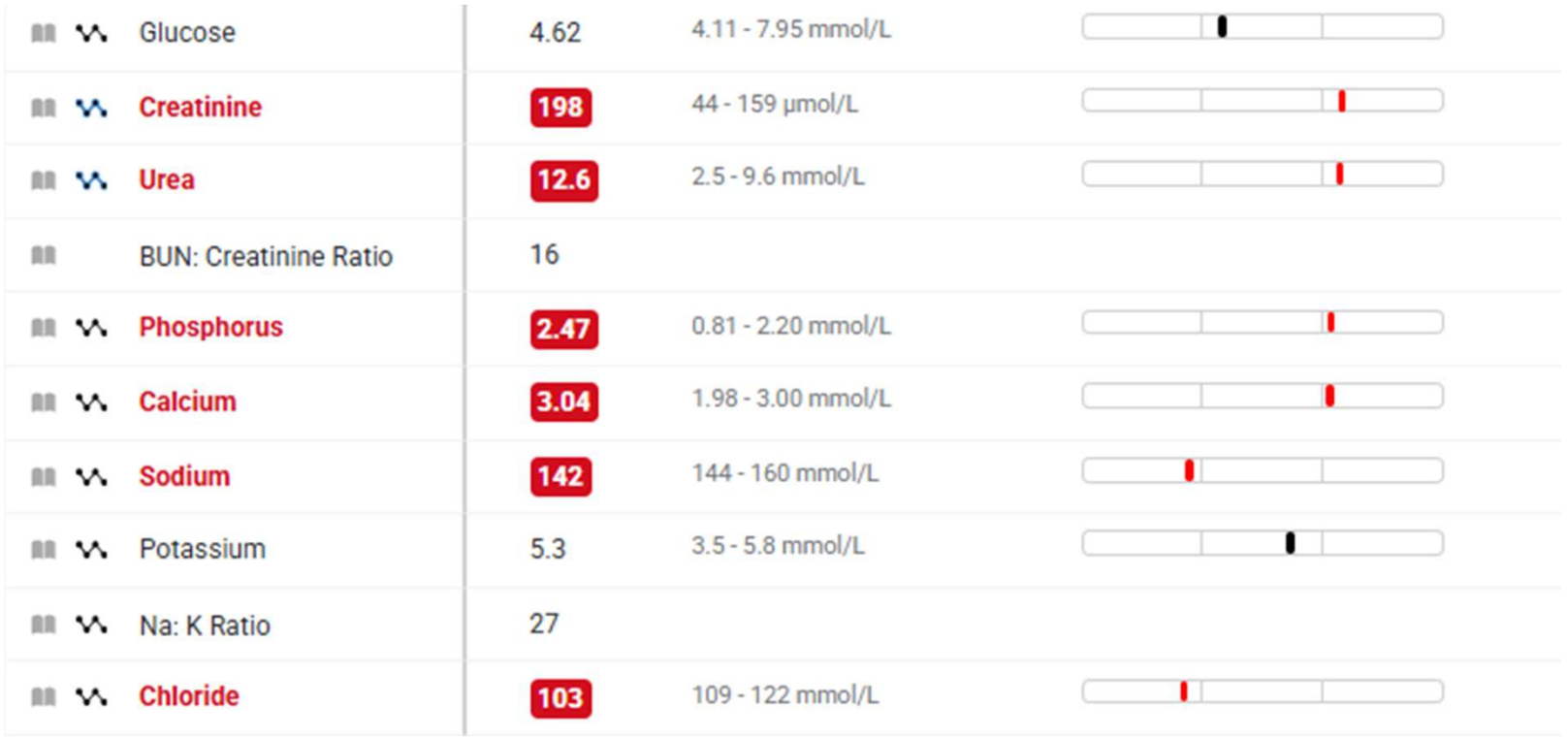
Serum biochemistry

+ Hyponatraemia, hypochloraemia, hyperkalaemia
+ Hypercalcaemia
+ Hypoglycaemia
+ Azotaemia



Glucose	4.62	4.11 - 7.95 mmol/L	
Creatinine	198	44 - 159 µmol/L	
Urea	12.6	2.5 - 9.6 mmol/L	
BUN: Creatinine Ratio	16		
Phosphorus	2.47	0.81 - 2.20 mmol/L	
Calcium	3.04	1.98 - 3.00 mmol/L	
Sodium	142	144 - 160 mmol/L	
Potassium	5.3	3.5 - 5.8 mmol/L	
Na: K Ratio	27		
Chloride	103	109 - 122 mmol/L	

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Haematology

RBC	6.85	5.65 - 8.87 x10^12/L	
Haematocrit	0.413	0.373 - 0.617 L/L	
Haemoglobin	156	131 - 205 g/L	
MCV	**60.3**	**61.6 - 73.5 fL**	L
MCH	22.8	21.2 - 25.9 pg	
MCHC	378	320 - 379 g/L	
RDW	17.5	13.6 - 21.7 %	
% Reticulocytes	0.5	%	
Reticulocytes	34.3	10.0 - 110.0 K/µL	
Reticulocyte Haemoglobin	28.9	22.3 - 29.6 pg	
WBC	11.06	5.05 - 16.76 x10^9/L	
% Neutrophils	46.9	%	
% Lymphocytes	32.4	%	
% Monocytes	11.2	%	
% Eosinophils	8.6	%	
% Basophils	0.9	%	
Neutrophils	5.19	2.95 - 11.64 x10^9/L	
Lymphocytes	3.58	1.05 - 5.10 x10^9/L	

+ Lack of stress leukogram

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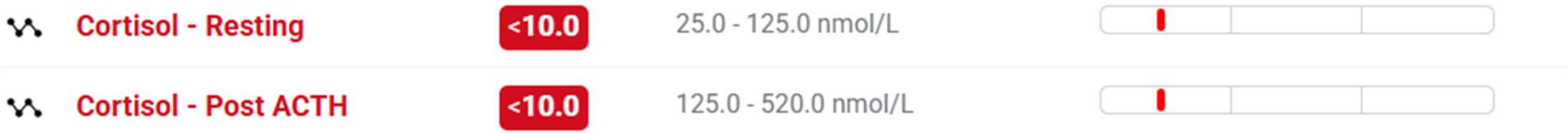
Basal cortisol and ACTH stimulation test

- Basal cortisol > 55nmol/L makes hypoadrenocorticism unlikely
  - But… from the dogs with basal cortisol < 55nmol/L only a minority have a diagnosis of hypoadrenocorticism
- ACTH stimulation test is the diagnostic test of choice



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Treatment hyponatremic and/or hyperkalemic hypoadrenocorticism

Acute Hypoadrenal Crisis

- IVFT
- Glucose +/- insulin +/- calcium gluconate
- Dexamethasone

Long-term therapy

- Prednisolone
  - 0.5mg/Kg while in hospital
  - Wean to usually around 0.05-0.1mg/Kg/day final dose
- Zycortal®
  - 1.5mg/kg PO every 28 days if>1y
  - Growing dogs may need higher dose

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.

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Monitoring long term treatment

- Glucocorticoids
  - Based on trial and error
  - ACTH stim test remains flat! Not useful in treatment monitoring!

- Mineralocorticoids / Zycortal®
  - Electrolytes at day 10 and day 28
  - Goal is to maintain potassium and sodium within reference range (RR) throughout between administrations
  - Electrolytes at day 10 assess peak effect of dose
  - Electrolytes at day 28 assess duration of dose

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

+ Day 10

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

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

+ Duration and/or dose of Zycortal® inadequate
+ Dose easier to change than duration
+ Dose needs to be increased by 10-20%

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What happens if electrolytes are abnormal at day 28?

+ Day 10

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

+ Day 28

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

+ Duration or dose of Zycortal® too high
+ No Zycortal® should be administered at day 28 given hypokalemia
+ Dose should be decreased by 10-20%

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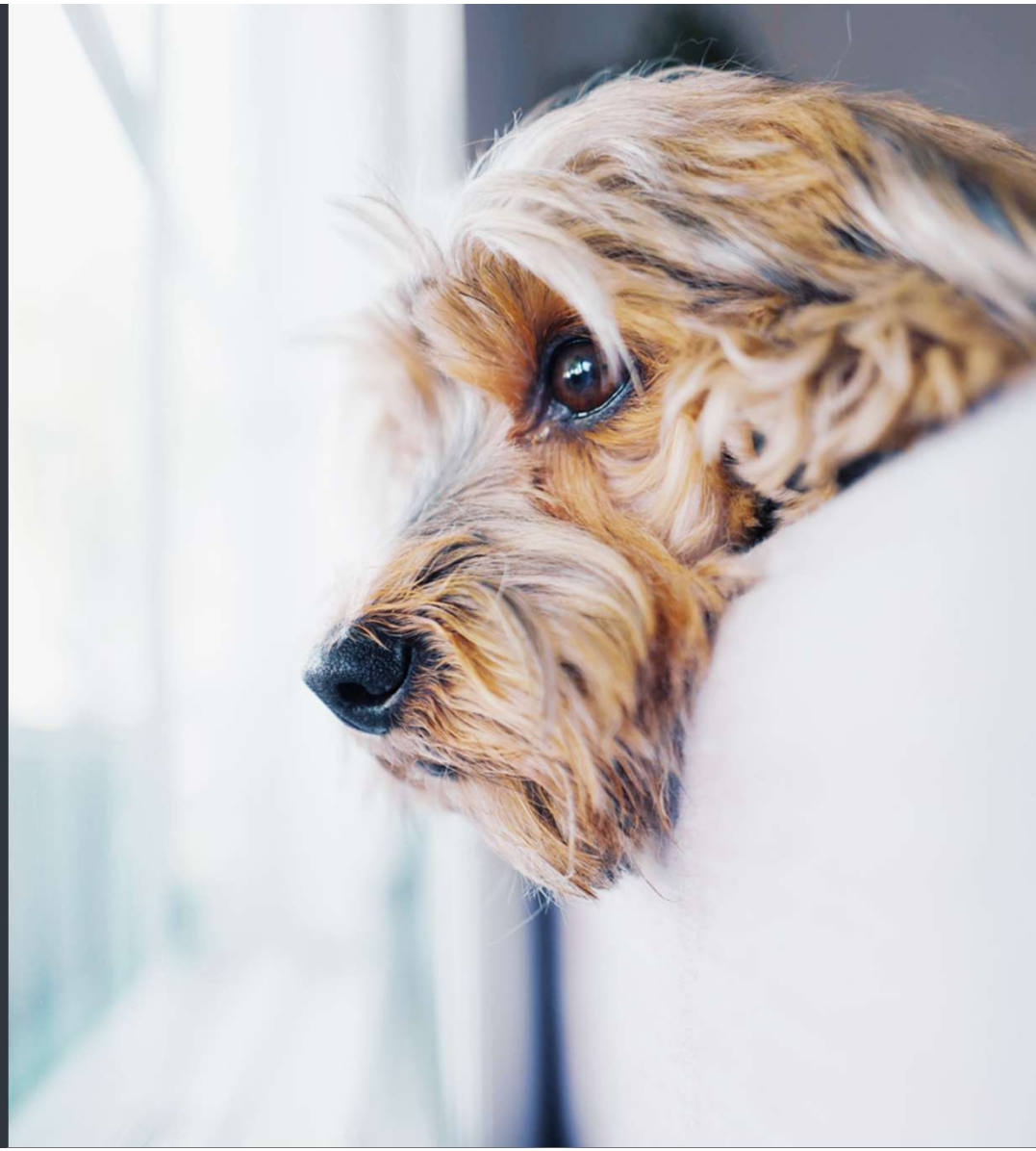
Thank You!

Any Questions?




IDEXX