



When Cushing's is Confusing: Adrenal FAQs

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IDEXX

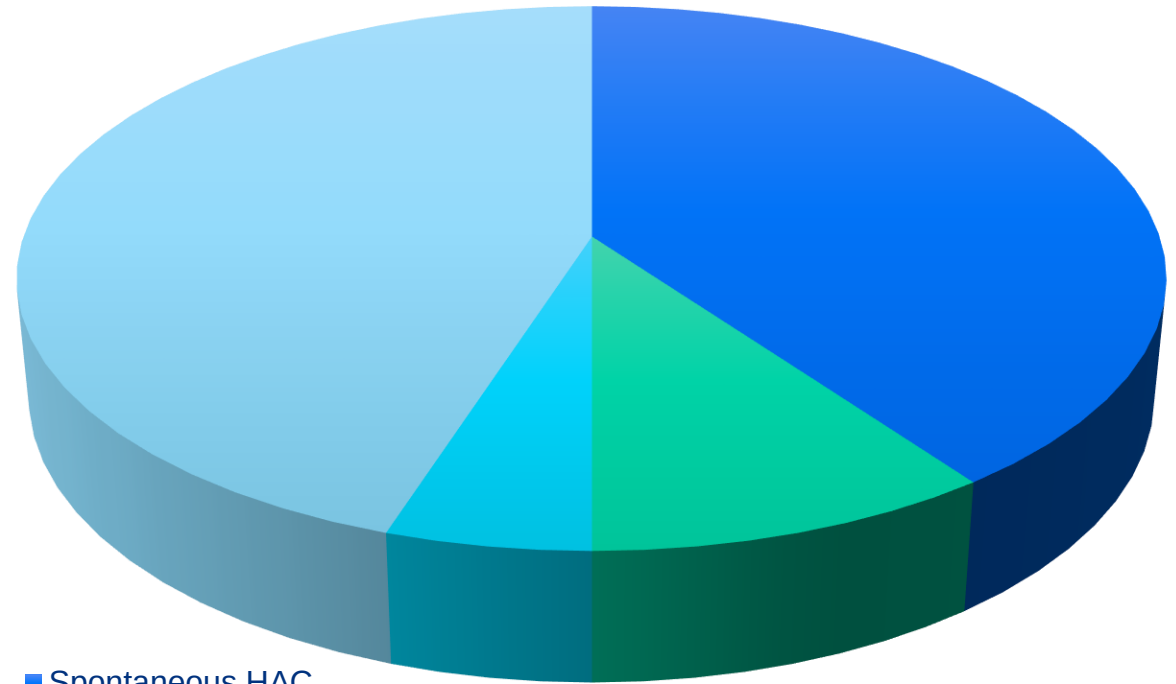
Conflicts of Interest & Disclaimer

- + Yvonne McGrotty is an employee of IDEXX Laboratories UK and also an employee of AniCura France.
- + Stephanie Sorrell is an employee of IDEXX Laboratories UK
- + *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.*

Hyperadrenocorticism (HAC).....Or is it??

Daily calls to IDEXX regarding HAC

- + One of the most common calls to IM service in IDEXX
- + Common endocrine disease in dogs
- + Many dogs are tested for HAC inappropriately
- + Inappropriate testing can lead to misdiagnosis



■ Spontaneous HAC

■ Iatrogenic HAC

■ I was testing for Addisons but now I think it might have HAC

■ Probably not HAC but tested for it anyway

Which is the 'best' test to rule out hyperadrenocorticism?

Which is the 'best' test to rule out HAC?

- + Clinical history!
 - + Signalment
 - + If PUPD is **not** present, then very unlikely to be hyperadrenocorticism
- + 'Screening' Tests
 - + UCCR
 - + Low dose dexamethasone suppression test



Cushing's Diagnostic Prediction Tool

Journal of Veterinary Internal Medicine

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STANDARD ARTICLE |  Open Access |    

Development and internal validation of a prediction tool to aid the diagnosis of Cushing's syndrome in dogs attending primary-care practice

Imogen Schofield , David C. Brodbelt, Stijn J. M. Niessen, David B. Church, Rebecca F. Geddes, Noel Kennedy, Dan G. O'Neill

First published: 16 September 2020 | <https://doi.org/10.1111/jvim.15851> | Citations: 1

First steps- Check for polydipsia/polydipsia

- + Normal H₂O intake
 - + 40-60mls/kg/day
- + Polydipsia
 - + >100 mls/kg/day in dogs
- + Don't test for HAC in patients that aren't PUPD
- + Urine SG <1.020



Further tests for HAC only
indicated once these tests
have been performed!
And only if Cx are supportive



Urine Cortisol:Creatinine (UCCR)

- + Good screening test (rules out HAC)
- + Urine MUST be collected by owner at home
- + False positives common
- + Non-specific
- + Positive result **MUST** be followed up by more specific testing

Can I use basal cortisol to diagnose HAC?



Basal Cortisol

- + Not useful for the diagnosis of HAC!
- + Episodic secretion
- + Fluctuates widely
- + Significant overlap with normal animals

🐾 **Cortisol -
Baseline**

171.0

25.0 - 125.0 nmol/L



🐾 Cortisol - Post
ACTH

356.0

125.0 - 520.0 nmol/L



Which is the better test to confirm HAC, the ACTH stim or the LDDST?

What is the best test to confirm HAC?

- + Clinical signs!
 - + PUPD
- + Supportive clin path results
- + Urinalysis confirming dilute urine
- + Only then can you choose a more specific confirmatory test

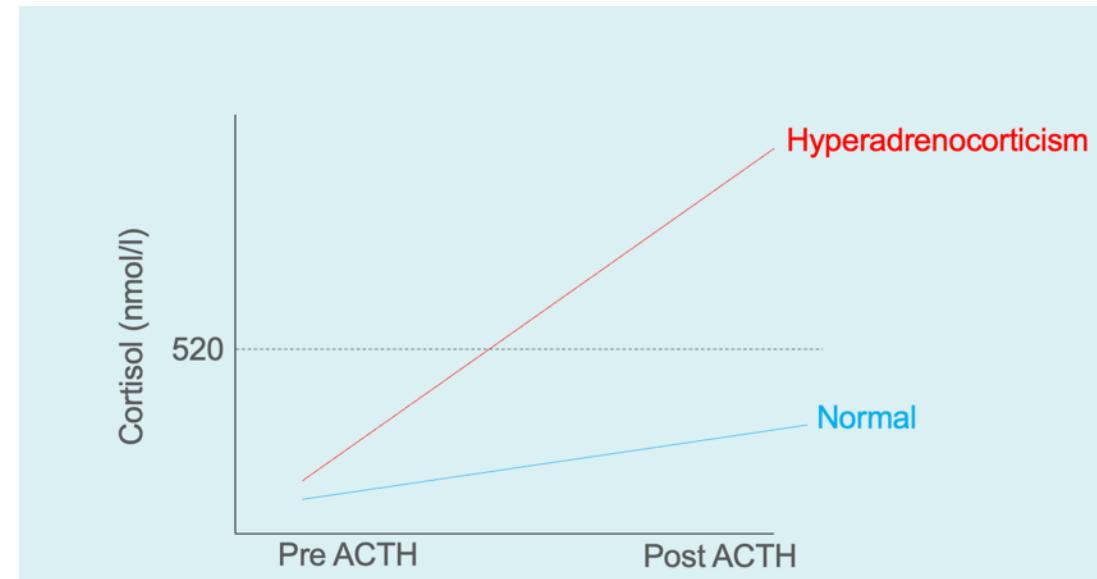


ACTH Stimulation Test Protocol

- + Fast for 12hrs
- + Sample for basal cortisol
- + Inject tetracosactide (Cosacthen)
 - + 5ug/kg IV
- + Obtain 2nd sample 1hr later
- + Measure cortisol on both samples

How Does ACTH Stimulation Test work?

- + Indirectly gauges degree of adrenocortical thickness
- + Dogs with HAC have increased thickness of adrenal cortex and have an exaggerated response to ACTH
- + Dogs with iatrogenic HAC have blunted response



Courtesy of Stephen Jordan

ACTH Stimulation Test

- + Not all dogs with HAC will test positive on ACTH stim
 - + Only around 50% of dogs with ADH test positive
 - + Around 80% of dogs with PDH test positive
- + False negatives
 - + Follow up with LDDST if HAC still seems clinically likely
- + False positives
 - + Stress of non-adrenal illness (up to 14%)

Cortisol - Baseline	149.0	25.0 - 125.0 nmol/L	
Cortisol - Post ACTH	803.0	125.0 - 520.0 nmol/L	

Advantages & Disadvantages of ACTH Stim Test

Advantages

- Quick and simple to perform
- Differentiates spontaneous from iatrogenic HAC
- Baseline information for therapeutic monitoring (trilostane/mitotane)

Disadvantages

- Poor sensitivity
- False negatives (especially with ADH)
- False positives (non-adrenal illness)
- Doesn't discriminate between PDH and ADH

Low Dose Dexamethasone (LDDS) Test Protocol

- + Fast the patient for 12 hours
- + Sample for basal cortisol (T=0)
- + Inject dexamethasone (0.015mg/kg) IV
- + Sample for cortisol at 4hrs and 8hrs after dexamethasone injection
- + Avoid stress for the duration of the test
 - + No other procedures



How do I interpret a LDDS test?

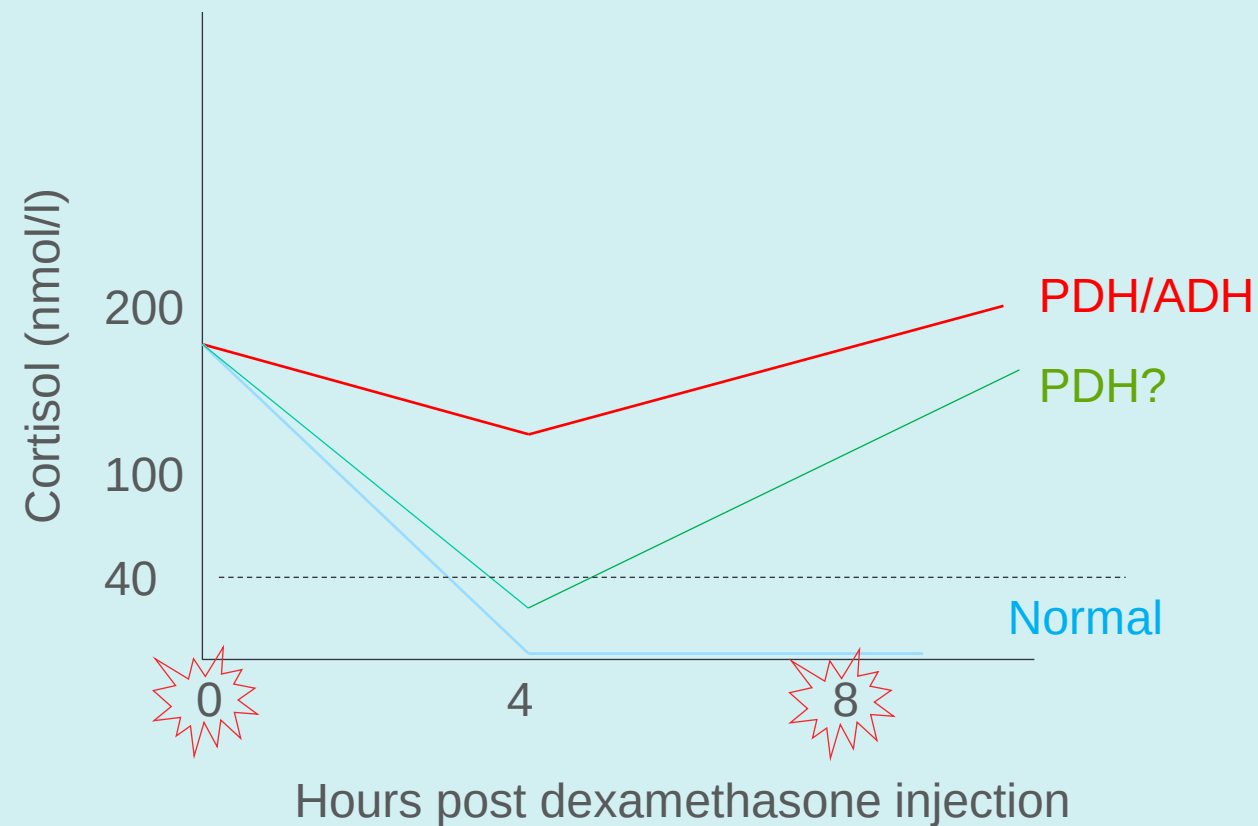
LDDS test

- + Dexamethasone is anticipated to suppress CRH and ACTH release for several hours and therefore reduce cortisol production
- + Assesses the entire hypothalamic-pituitary-adrenal axis
- + ADH – cortisol secretion is **not** expected to be suppressed
- + PDH – cortisol secretion **may or may not** be suppressed

Canine Hyperadrenocorticism



Low dose dexamethasone suppression test



How do I interpret a LDDS test?

- + First look at the 8hr result
- + If it's less than 40nmol/l then it is NOT supportive of HAC

 Cortisol - Baseline	146.0	25.0 - 125.0 nmol/L	
Cortisol - 4 hr Post Dex	<10.0	nmol/L	
Cortisol - 8 hr Post Dex	<10.0	<= 40.0 nmol/L	

How do I interpret a LDDS test?

- + First look at 8hr sample
 - + Not fully suppressed
 - + Consistent with HAC where there are supportive signs and clinpath changes
- + Then look at 4hr sample
 - + Suppression at 4hrs present here- consistent with pituitary dependent HAC
 - + (not all pituitary HAC cases show suppression at 4hrs)
 - + (adrenal dependent cases don't suppress at all)

 Cortisol - Baseline	85.3	25.0 - 125.0 nmol/L	
Cortisol - 4 hr Post Dex	11.6	nmol/L	
Cortisol - 8 hr Post Dex	78.9	<= 40.0 nmol/L	

Advantages & Disadvantages of LDDS

Advantages

- + Good screening test
 - + 90-95% dogs with PDH test positive
 - + Almost 100% ADH
- + May confirm PDH
 - + Suppression at 3-4hrs

Disadvantages

- + Low specificity
 - + Especially in sick dogs (40-50%)
 - + More likely to produce false positives
- + Takes longer to perform (8hrs)

Comparison of Tests- Neither test is ideal!

ACTH Stim

- + Quick test (1hr)
- + Low sensitivity
 - + High rate of false negatives
- + Moderate risk of false positives
 - + Especially diabetes mellitus
- + Tests for iatrogenic HAC

LDDS Test

- + Long test (8hrs)
- + High sensitivity
 - + Low rate of false negatives
- + Lower specificity
 - + Risk of false positives
- + Does not test for iatrogenic HAC

Can I sedate a dog before running an ACTH stim or LDDS test?

Can I sedate a dog before running an ACTH stim or LDDS test?

- + Best to avoid sedation
- + Trazodone decreases cortisol levels in healthy dogs



[J Vet Intern Med.](#) 2024 Jan-Feb; 38(1): 130–134.

PMCID: PMC10800203

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PMID: [37965773](https://pubmed.ncbi.nlm.nih.gov/37965773/)

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

[Morgan Brown](#),¹ [Tekla Lee-Fowler](#),¹ [Ellen N. Behrend](#),¹ and [Megan Grobman](#)^{1, 2}

Can I run an ACTH stim on a dog receiving steroids?

Can I run an ACTH stim on a dog receiving steroids?

- +Yes.....but what would be the point?

- +It confirms the dog is taking steroids!
- +Adrenal suppression expected- flatline response
- +May also cross react with assay



How long do I need to taper the steroids for before testing for Cushing's?

How long do I need to taper the steroids for?

- + Very little published information
- + Steroids suppress adrenal axis & cross react with the assays too
- + This question depends on multiple patient factors so best to call to discuss



How do I monitor response to trilostane if the owner is giving the tablet at night?

How do I monitor response to trilostane if the owner is giving the tablet at night?

- + Simply set your alarm for midnight.....or.....
- + Change to morning dosing:
 - + Wait a week after a change in time of administration before monitoring
 - + ACTH stim 4-6h post pill
 - + Pre pill cortisol immediately before tablet is given



When should I collect the sample for a pre-pill cortisol assay?

When should I collect the sample for a pre-pill cortisol assay?

- Before the pill!
- So, if given at 9am in the morning, at around 9am before the owner gives the medication



Can I monitor trilostane therapy with the LDDS test?

Can I monitor trilostane therapy with LDDS test?

- No



- Trilostane is already suppressing the adrenal axis
- Our goal is to monitor the adrenals' ability to respond to stress, so a stimulation test is needed

Pre-anaesthetic blood tests for routine dental work show increased ALP- which test should I do next?

Screening blood tests show increased ALP- which test should I do next?

- No dog has ever died of an increased ALP
- Only perform tests for HAC if there are supportive clinical signs
- Consider also
 - Benign nodular regeneration of the liver
 - Very common in older dogs
 - Gall bladder disease



How do I test for Cushing's in a diabetic dog?

How do I test for Cushing's in a diabetic dog?

- + Step away from the tetracosactide!
- + Clinical signs and biochemical changes very similar
 - + ALP, ALT, chol
- + Wait until diabetes stabilised before considering testing for HAC
 - + Usually takes at least 3mths to stabilise a diabetic
 - + High risk of false positive if testing performed on an unstable diabetic
 - + Need for high dose insulin to achieve stability should raise suspicion of concurrent HAC



Any Questions?

“The only stupid question is
the question that is never
asked”

