When Cushing's is Confusing: Adrenal FAQs

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Conflicts of Interest & Disclaimer

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

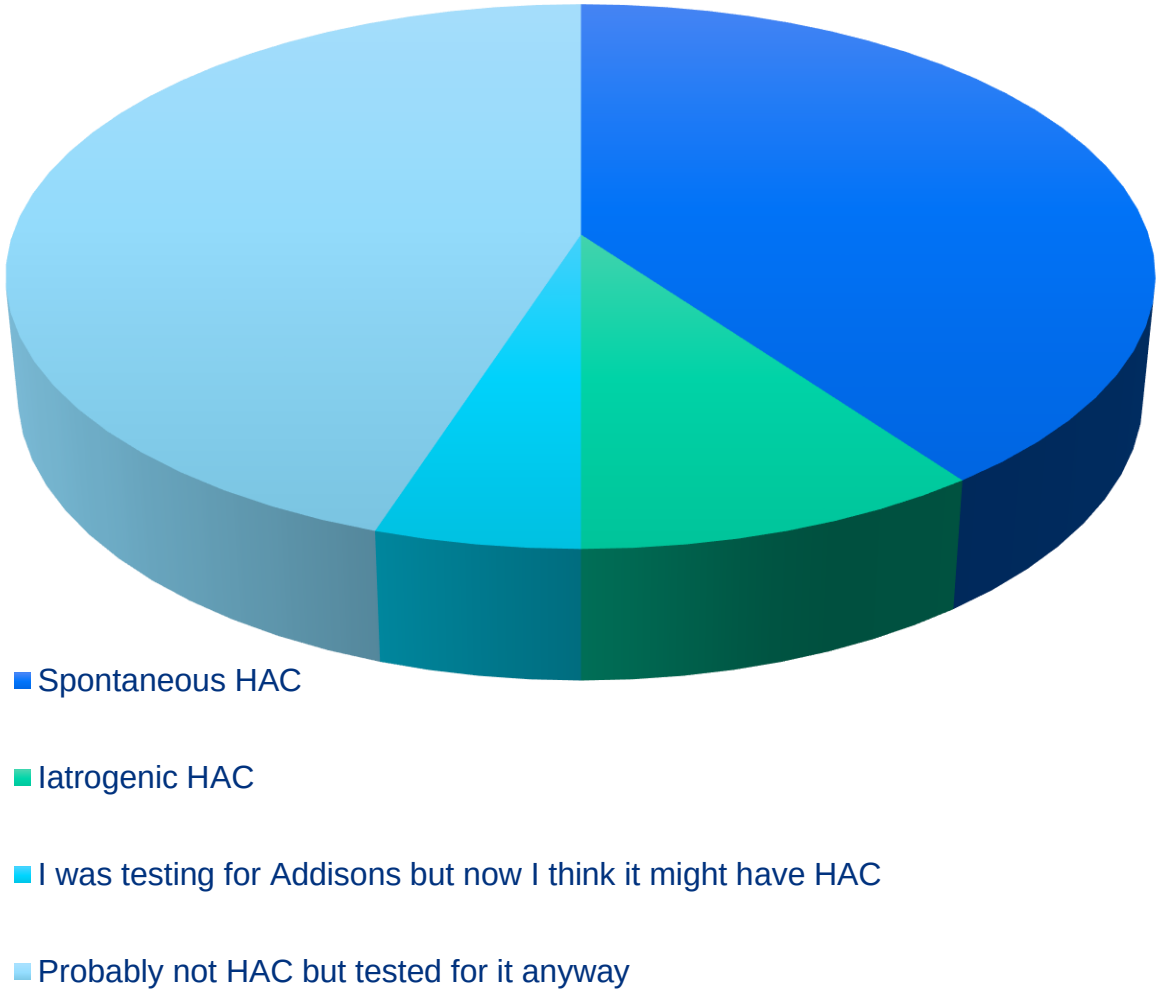
+ Stephanie Sorrell is an employee of IDEXX Laboratories UK

+ *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??

- 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

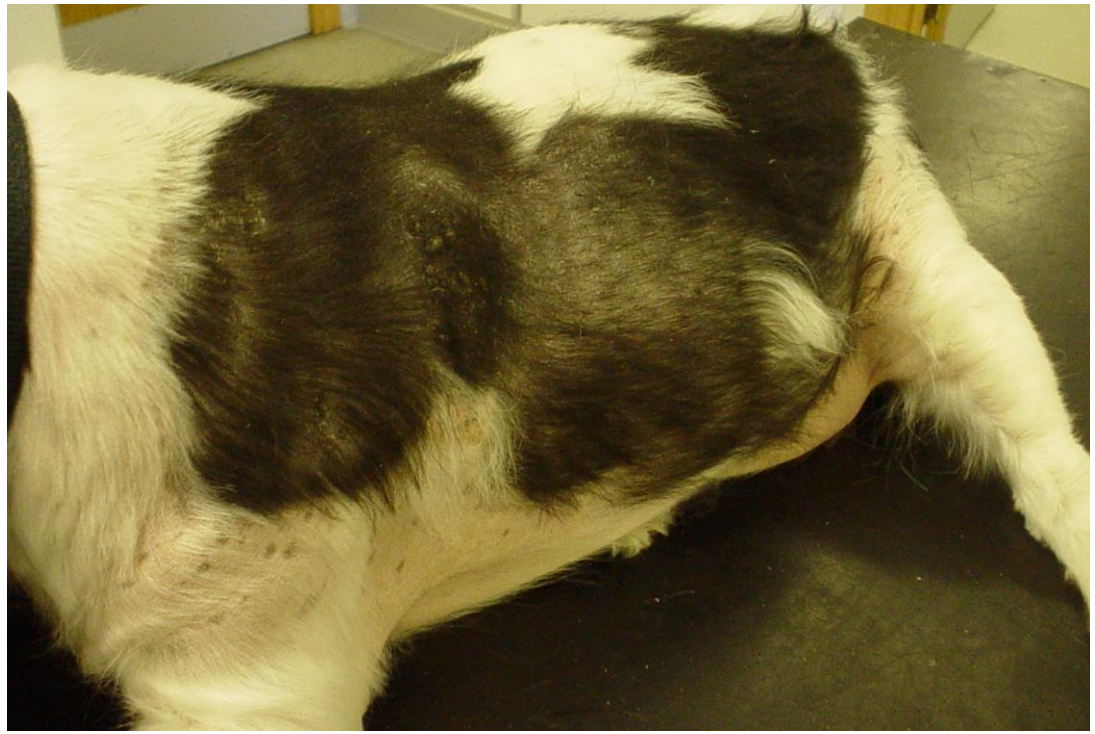
Daily calls to IDEXX regarding HAC



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
Open Access
ACVIM

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

IDEXX

First steps- Check for polydipsia/polydipsia

- Normal H_2O 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	

IDEXX

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

What is the best test to confirm HAC?

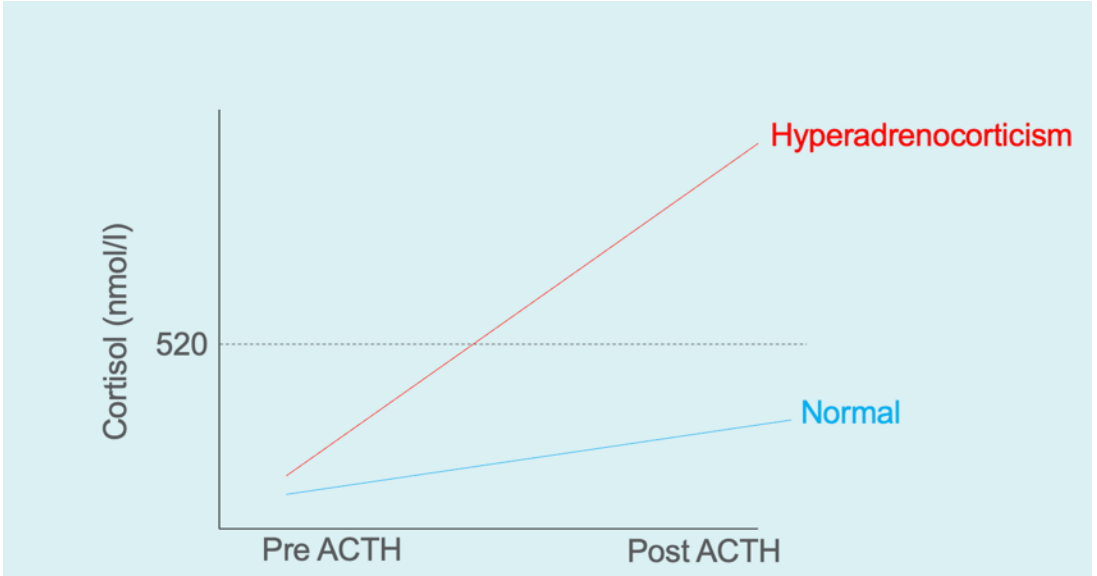
- Clinical signs!
  - PUPD
- Supportive clin path results
- Urinalysis confirming dilute urine
- Only then can you choose a more specific confirmatory test

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

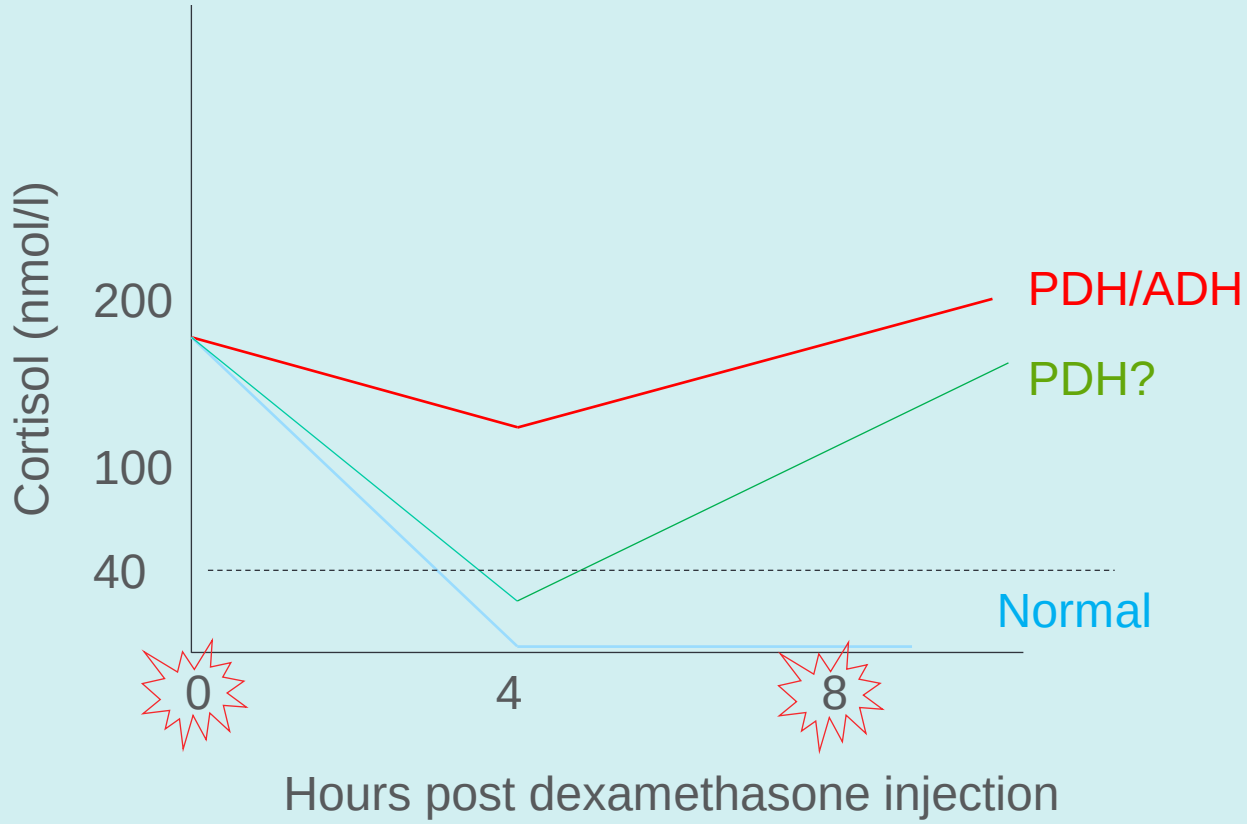
- Assesses the entire hypothalamic-pituitary-adrenal axis

- 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



Courtesy of Stephen Jordan

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.
Published online 2023 Nov 15. doi: 10.1111/jvim.16935
PMCID: PMC10800203
PMID: 37965773

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] 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”