
VMX
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Festival of the HeARTS
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HAC...easy as 1, 2, 3. Simplifying Cushing's diagnosis and management.

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Conflict of Interest Disclosure

I have financial interest, arrangement or affiliation with:

Idexx, Boehringer Ingelheim:	**Consultant, honoraria**
Merck Animal Health, Dechra Pharmaceuticals:	**Honoraria**

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Conflict of Interest Disclosure:

Full-time IDEXX Employee

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Cushing's Syndrome FAQs

- What's the best way to diagnose Cushing's?
- My dog looks/acts cushingoid but the LDDST is normal, now what?
- Does atypical Cushing's exist?
- Do I have to differentiate between pituitary and adrenal disease?
- What if I don't treat?
- What is the starting dose of trilostane?
- Do we need an ACTH stim test to monitor therapy?

What do we call it nowadays?

ALIVE: Agreeing Language In Veterinary Endocrinology

Then and now…

Cushing's disease, hyperadrenocorticism

Pituitary-dependent hypercortisolism

Adrenal-dependent hypercortisolism

Atypical Cushing's disease

Cushing's syndrome

ACTH-dependent Cushing's syndrome

ACTH-independent Cushing's syndrome

Subdiagnostic Cushing's syndrome*

*Can be ACTH-dependent or ACTH-independent

What's the best way to make the diagnosis?

Right patient, LDDST, abdominal ultrasound.

Cushing's *syndrome* for a reason

- ***Clinical*** **syndrome due to chronic glucocorticoid excess**
- **More false positives if screen wrong patient (low pretest probability)**
- **Higher pretest probability of disease with:**
  - ***Multiple*** **supportive clinical and laboratory signs: typical plus…**
    - **Hypertension**
    - **Thrombocytosis, hypercholesterolemia, mild hyperglycemia, proteinuria**
    - **ALT > ALP more likely primary liver disease**

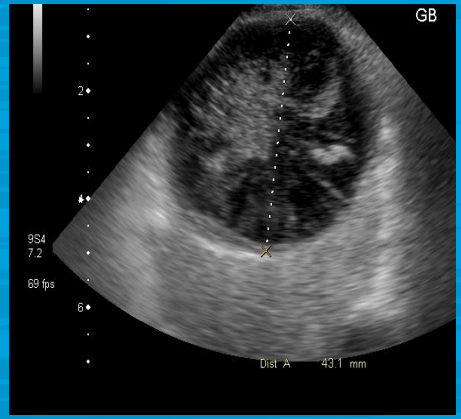
Why LDDST first to screen?

A good screening test has high sensitivity (fewer false negs)

- **Sensitivity**
  - **UCCR 99%**
  - **LDDST 95%**
  - **ACTH Stim 80%**
- **Specificity**
  - **ACTH stim 90%**
  - **LDDST 71%**
  - **UCCR 25%**

Abdominal ultrasound

- Adrenomegaly
  - >0.7-0.75 cm, >0.6 cm small dogs
  - Unilateral
  - Bilateral
  - Incidentaloma?
- Hepatomegaly
- Gallbladder mucocele 30X more likely in dogs with Cushing's



Does 4-hr sample matter?

- *

The dog looks/acts cushingoid but the LDDST is normal, now what?

Call Dr. Lathan.

Suspect Cushing's but LDDST negative

- Any screening test can be negative when Cushing's present
  - Wrong (i.e., high) dose of dexamethasone?
  - Mild disease?
- Evaluate for other causes of signs.
- Retest now with different test if strongly suspect
- Retest in 3-6 months if signs mild and no complications, e.g., hypertension, proteinuria….

How far do I go in pursuing ‘atypical Cushing’s?

Well now you’ve opened a can of worms...

Name change - subdiagnostic Cushing’s syndrome.

Subdiagnostic may just be mild ‘typical’

- Cut-offs established decades ago
- Vary from lab to lab (as do cortisol assays)
- May be too high
- Normal animals have 4- and 8-hr cortisol values at or below detection limit

Subdiagnostic may just be mild typical HAC

The case for re-evaluating (lowering) cut-offs

8 hr cortisol (ug/dL)	Lab A cut-off 1.5 ug/dL	Lab B cut-off 1.0 ug/dL	Lab C cut-off 0.6 ug/dL
1.7	HAC	HAC	HAC
1.3	Normal	HAC	HAC
0.8	Normal	Normal	HAC
0.5	Normal	Normal	Normal

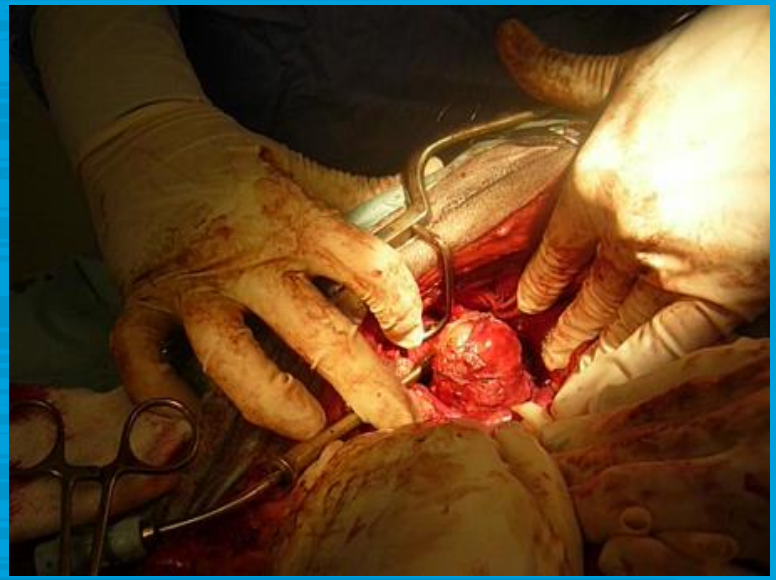
Do I have to differentiate between pituitary and adrenal disease?

Yes, please.

BUUUUUUUUT…

Differentiating PDH vs. ADH important
(Some dogs have both)

- Treatment and prognosis differ
- Surgery curative
  - Hypophysectomy or adrenalectomy
- Differentiating test only after positive screen
- Abdominal ultrasound used most, HDDST
  - 20-25% PDH do not suppress with HDDST
  - Diagnose PDH and AT in same dog
- eACTH most accurate stand-alone test but overlap and sample handling limit use



What if I don't treat…?

Journal of Veterinary Internal Medicine

ACVIM
American College of Veterinary Internal Medicine

Open Access

Standard Article

J Vet Intern Med 2017;31:22–28

Comparison of Survival Times for Dogs with Pituitary-Dependent Hyperadrenocorticism in a Primary-Care Hospital: Treated with Trilostane versus Untreated

N. Nagata, K. Kojima, and M. Yuki

Withholding trilostane increased risk of death

- Trilostane treatment 17 dogs
- No trilostane 26 dogs
- Hazard ratio 5.01 in untreated
- 2 yr survival
  - Trilostane 52.2%
  - No treatment 8.5%
- Controlling cortisol excess important
  - Less risk of pulmonary thromboembolism, diabetes mellitus, acute pancreatitis, systemic hypertension, infection, gallbladder mucocele
  - Better QOL

What is the starting dose of trilostane?

Glad you asked…

Cushing's syndrome: Treatment

- Trilostane 0.5-1.5 mg/kg q12h
  - Survival longer with q12h dosing
  - BW > 25 kg may need lower dose
- Name brand product only
  - Potency of compounded formulations variable
- Not free of side effects
  - Hypoadrenocorticism usually transient
  - Adrenal necrosis, idiosyncratic, not dose-dependent, permanent or transient
  - Hyperkalemia and/or hyponatremia despite adequate control of cortisol

Do I need to do an ACTH stim to monitor treatment?

Usually not.

Clinical well-controlled dogs

- Pre-pill cortisol <1.4-2 µg/dL
  - ↓ dose by 10-20% OR ACTH stim
- Pre-pill cortisol >1.4-2 µg/dL
  - Continue current dose
- Pre-pill cortisol >7 µg/dL
  - Re-evaluate history, USG, SID vs BID
  - CONSIDER small dose increase, based on CS/USG
    - Owner considerations

Clinically Uncontrolled Dogs

- Pre-pill cortisol >5 µg/dL
  - Increase dose or split to BID
- Pre-pill cortisol 1.4-5 µg/dL (Grey zone)
  - Split dose if SID
  - Maybe increase dose if >….3 µg/dL?
  - Consider concurrent dz (DM?), stim <3 µg/dL ?
- Pre-pill cortisol <1.4-2 µg/dL
  - Re-evaluate history, perform ACTH stim, +/- other diagnostics, consult with an internist

Thank you!

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