VITICUSGROUP™
WVC ANNUAL CONFERENCE
MARCH 2 - 5, 2025 | LAS VEGAS, NV

HAC…easy as 1, 2, 3.
Simplifying Cushing's syndrome diagnosis and management.

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IDEXX

Financial Disclosure

Patty Lathan

I have financial interest, arrangement or affiliation with:

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

Bill Saxon

Full-time IDEXX Employee

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…

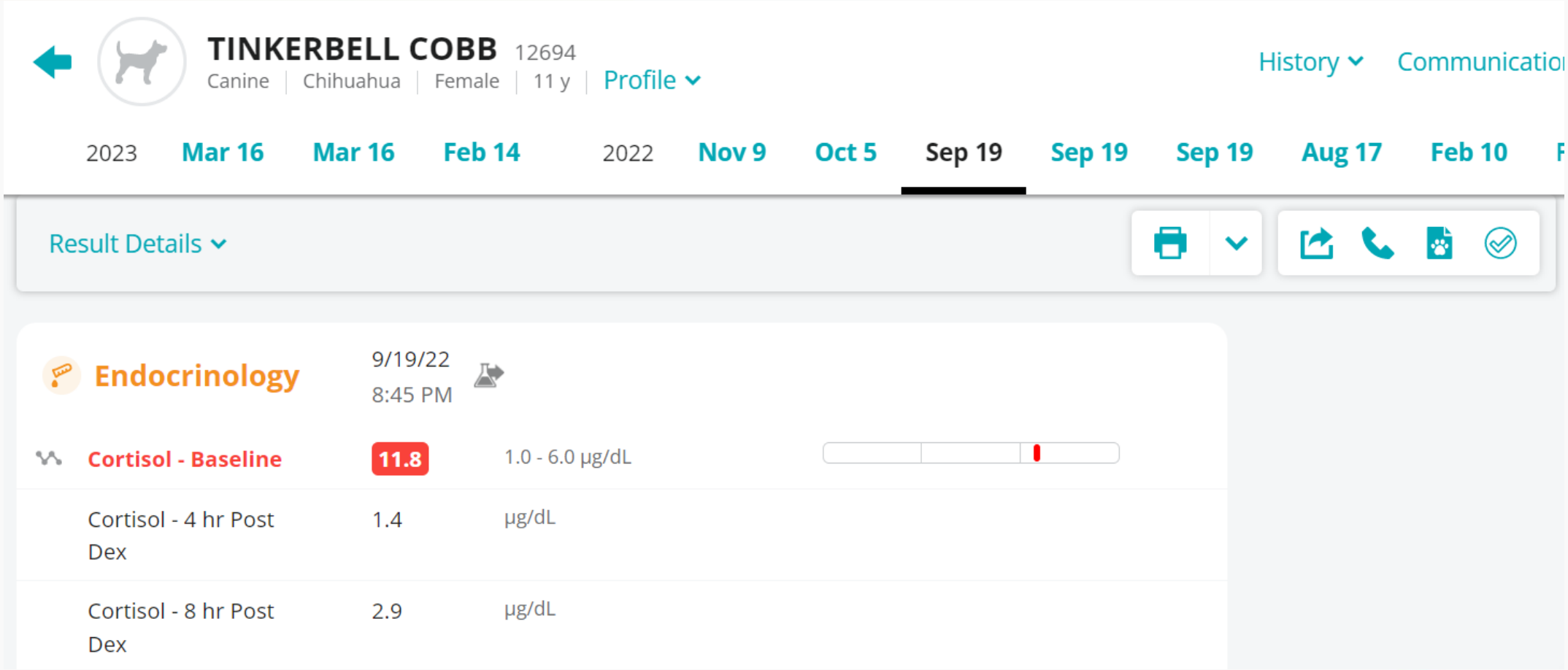
Cushing's disease or hyperadrenocorticism (HAC)	Cushing's syndrome
Pituitary-dependent hyperadrenocorticism	Pituitary-dependent hypercortisolism OR ACTH-dep hypercortisolism
Adrenal-dependent hyperadrenocorticism	Adrenal-dependent hypercortisolism OR ACTH-indep hypercortisolism
Atypical Cushing's disease	Subdiagnostic Cushing's syndrome

What's the best way to diagnose Cushing's in a patient without significant concurrent disease?

Right patient, LDDST, abdominal ultrasound.

LDDST interpretation

(0.01 mg/kg dexamethasone IV then 0, 4, 8 hr cortisol)



Cushing's *syndrome* for a reason

- ***Clinical*** **syndrome due to chronic glucocorticoid excess from any cause**
- **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?

Screening test should have high sensitivity (few false negs)

- **Sensitivity**
  - **UCCR 99%**
  - **LDDST 95%**
  - **ACTH Stim 60-80%**
- **Specificity**
  - **ACTH stim 90%**
  - **LDDST 71%**
  - **UCCR 25%**

LDDST: Screening Interpretation

(***USE YOUR LAB'S NUMBERS!)

1. DO NOT look at the 4 hr result for screening!
2. Look at 8 hr result

→ IF cortisol >1.4 µg/dL

→ Consistent w/ HAC

LDDST: Differentiation Interpretation

(USE YOUR LAB'S NUMBERS!)

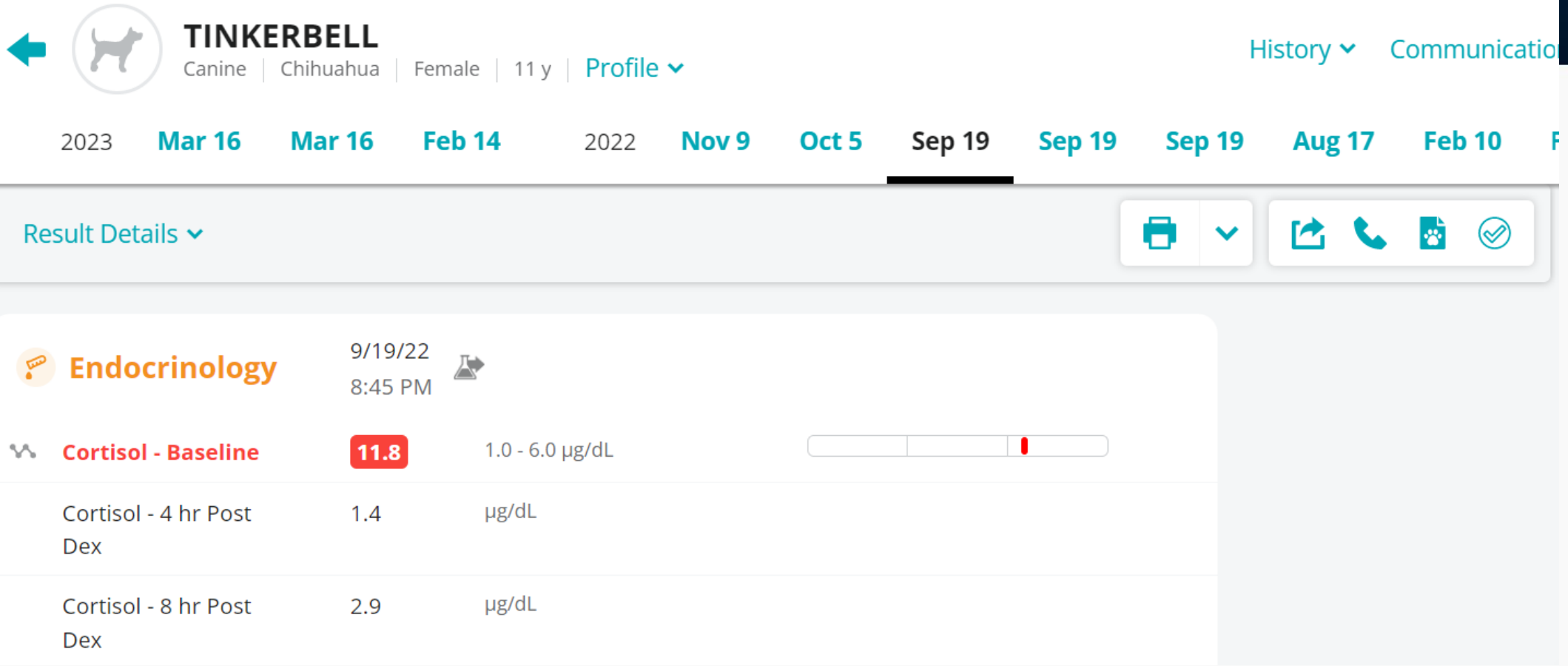
PDH if: **4 hr < 1.4 µg/dL OR**

4 hr < ½ baseline OR

8 hr < ½ baseline

35% of PDH dogs DO NOT FIT THESE CRITERIA!!!

CANNOT RULE-OUT PDH BASED ON LDDST!!!


TINKERBELL
Canine | Chihuahua | Female | 11 y | Profile
History
Communicatio
2023
Mar 16
Mar 16
Feb 14
2022
Nov 9
Oct 5
Sep 19
Sep 19
Sep 19
Aug 17
Feb 10
Result Details
Endocrinology
9/19/22
8:45 PM
Cortisol - Baseline
11.8
1.0 - 6.0 µg/dL
Cortisol - 4 hr Post Dex
1.4
µg/dL
Cortisol - 8 hr Post Dex
2.9
µg/dL

PERUA
Canine | Bichon Frise | Female | 12 y | Profile

2023 **Jan 24** 2022 **Dec 27** **Dec 16** **Dec 10**

Communicati **Feb 4**

Result Details

Endocrinology

12/27/22
1:15 AM

Cortisol - Baseline	a.	3.2	1.0 - 6.0 µg/dL
Cortisol - 4 hr Post Dex	b.	3.7	µg/dL
Cortisol - 8 hr Post Dex	c.	5.9	µg/dL

DecisionIQ Graphing

Expand All | Collapse All

Dexamethasone Suppression Interpretation

0.01 mg/kg

Yes, clinical signs present

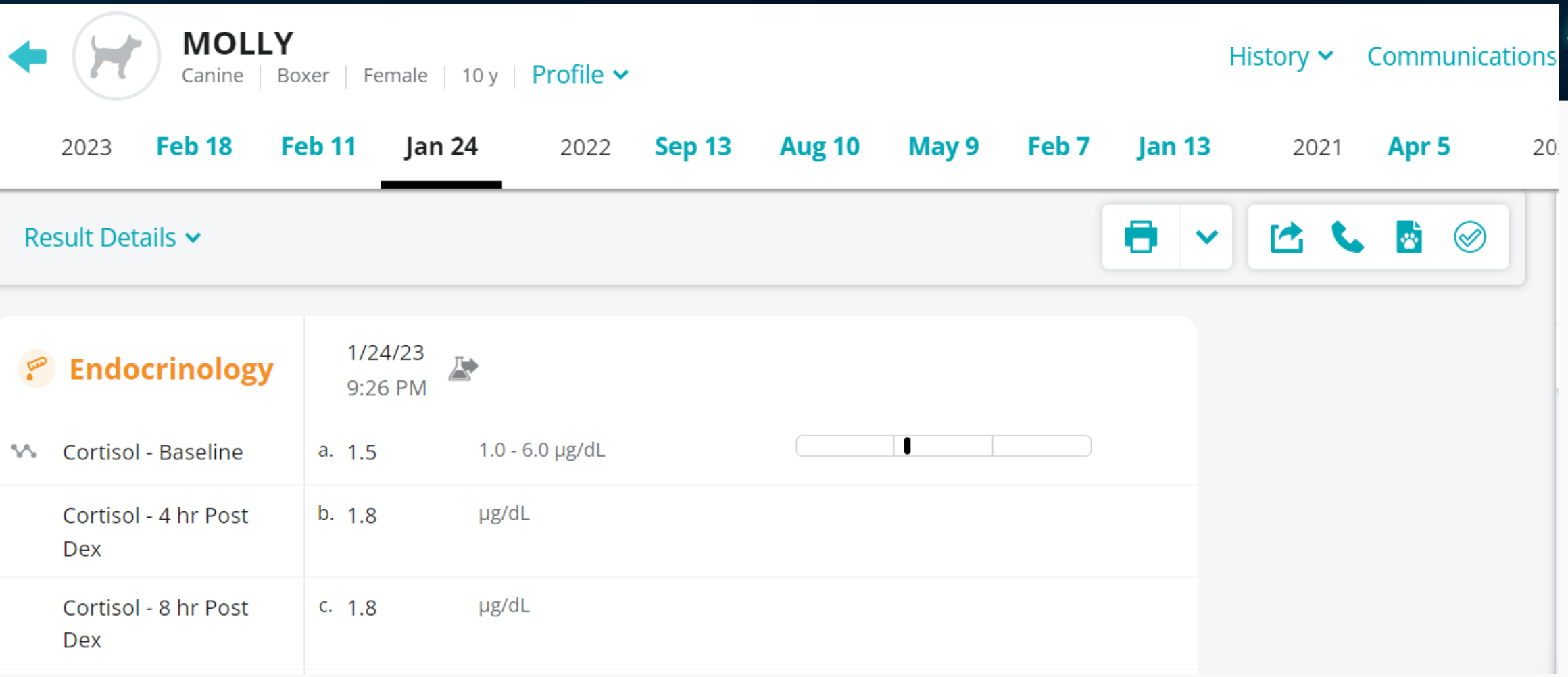
The result of the low dose dexamethasone suppression (LDDS) test in this dog **supports** a diagnosis of hyperadrenocorticism and **does not differentiate** pituitary-dependent from adrenal-dependent disease.

NEXT STEP CONSIDERATIONS

In a dog with clinical signs consistent with hyperadrenocorticism, it is recommended to pursue differentiation of pituitary-dependent from adrenal-dependent disease by performing either an abdominal ultrasound, high-dose dexamethasone suppression (HDDS) test, and/or an endogenous ACTH concentration. If the dog has concurrent illness (i.e. diabetes mellitus), consider first managing the concurrent disease and then repeating the LDDS prior to performing additional differentiating tests.

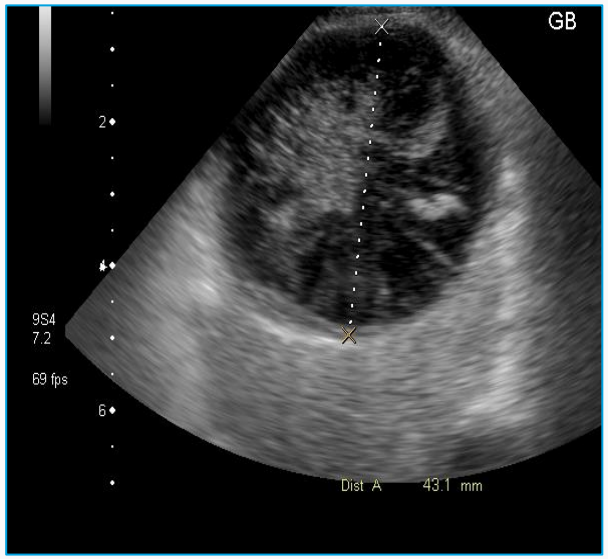
Please note that administration of exogenous steroids or stress related to concurrent illness may affect the results and interpretation of the dexamethasone suppression test.

Are you satisfied with this tool?


MOLLY
Canine | Boxer | Female | 10 y | Profile
History
Communications
2023 Feb 18 Feb 11 Jan 24 2022 Sep 13 Aug 10 May 9 Feb 7 Jan 13 2021 Apr 5
Result Details
Endocrinology
1/24/23
9:26 PM
Cortisol - Baseline
a. 1.5
1.0 - 6.0 µg/dL
Cortisol - 4 hr Post Dex
b. 1.8
µg/dL
Cortisol - 8 hr Post Dex
c. 1.8
µg/dL

Abdominal ultrasound next

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



My 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 disease(s) as cause of signs.
- Strongly suspect (or complications*) → retest now with different test
  - ACTH stimulation test
- Mild signs (no complications) → repeat LDDST in 3-6 months

* systemic hypertension, proteinuria, recurrent infection…

Does atypical Cushing's exist?

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

Name change - subdiagnostic Cushing's syndrome.

Subdiagnostic may just be mild ‘typical’

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

Subdiagnostic may just be mild/early ‘typical’

- Cortisol cut-offs established decades ago

- **May be too high**
- **Vary from lab to lab (as do cortisol assays)**
- **Normal animals have VERY LOW 4- and 8-hr cortisol values**

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

Normal dog should be <1

If not lower…

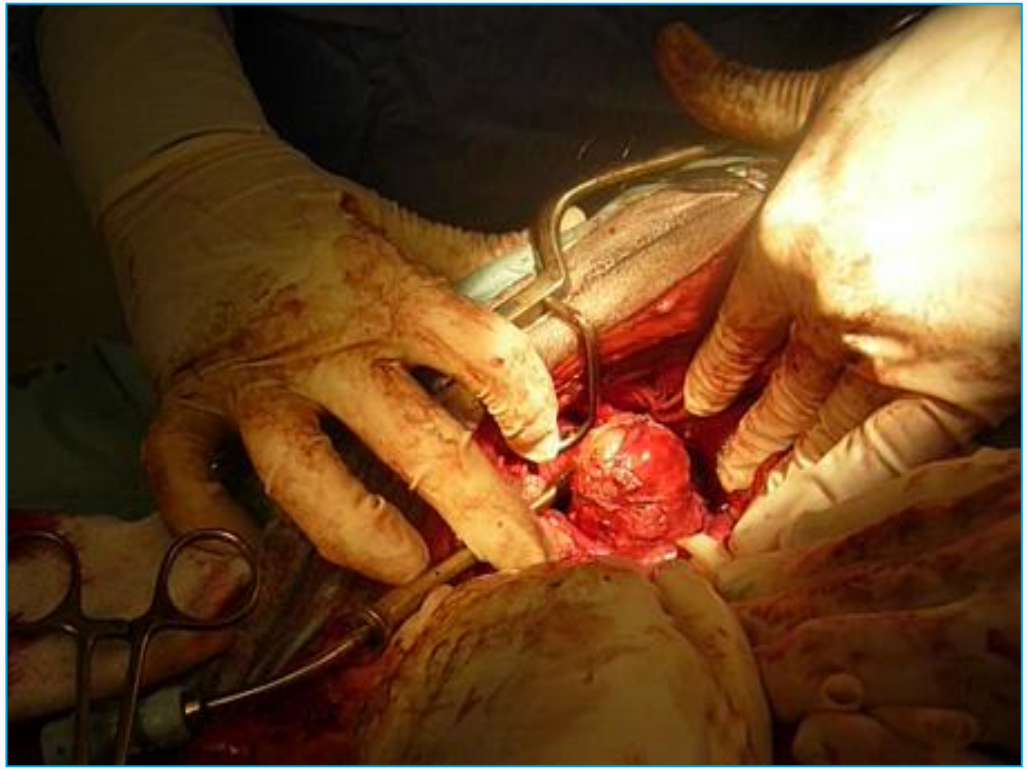
Do I *have* to differentiate between pituitary and adrenal disease?

Yes, please.

BUUUUUUUUT…

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

- **Treatment and prognosis differ**
- **Surgery curative**
  - **Hypophysectomy, adrenalectomy**
- **Differentiating test only after positive LDDST**
- **Abdominal ultrasound >>>> HDDST**
  - **AUS can diagnose PDH and AT in same dog**
  - **20-25% PDH dogs do not suppress w HDDST**
- **eACTH most accurate stand-alone test**
  - **Overlap and special handling limit use**



Journal of Veterinary Internal Medicine

ACVIM American College of Veterinary Internal Medicine

Open Access

Standard Article

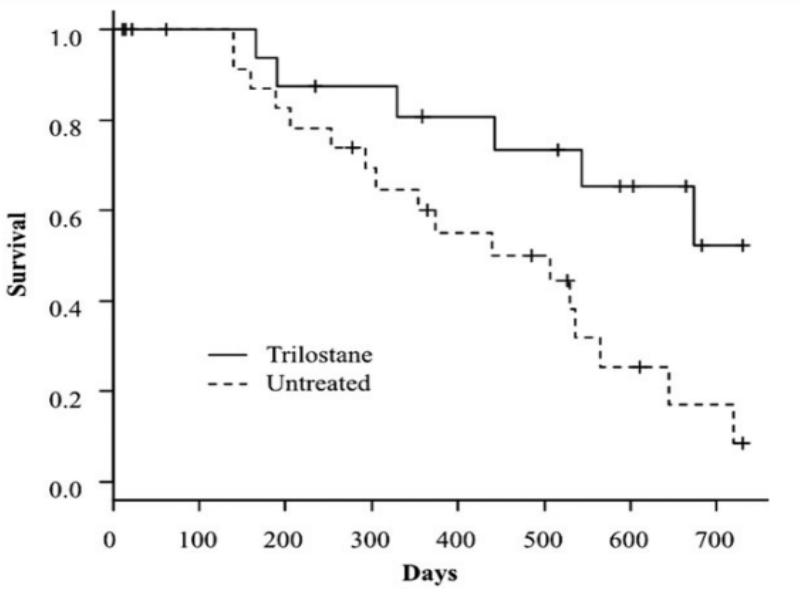
J Vet Intern Med 2017;31:22–28

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
- 2 yr survival
  - Trilostane 52.2%
  - No treatment 8.5%
- Controlling cortisol excess important
  - ↓ risk of PTE, DM, acute pancreatitis, hypertension, infection, 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.

Clinically 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

Do I need to worry about this in cats?

If you're Dr. Lathan you do…

Suspect Cushing's syndrome in a cat if:

- DERM changes: skin hyper fragility syndrome (≈30%)
- Pendulous abdomen
- Folded ear tips (weak cartilage) rare but specific
- PU/PD (caused by concurrent diabetes, not Cushing's)
- No panting
- Increased BG, cholesterol, ALP (lipidosis, not steroid-induced)
  - ALP increase NOT as common in cats as dogs
- Skin changes more common than over diabetes mellitus

Cushing's syndrome in cats: diagnosis/treatment

- LDDST using 0.1 mg/kg IV, 0, 4, 8 hr sample like dogs
- Abdominal ultrasound to differentiate
- Cure if possible – adrenalectomy, hypophysectomy, radiation
- Trilostane 5 mg BID usually
  - Reported range 1-2 mg/kg q8-12h with food

Thank you!