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Addison's disease: Don't make a 'crisis' out of diagnosis and management.

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Conflict of Interest Disclosure

I have financial interest, arrangement or affiliation with:

Idexx, Boehringer Ingelheim, Scout Bio:

Consultant, honoraria

Merck Animal Health, Dechra Pharmaceuticals:

Honoraria

Bill Saxon

Conflict of Interest Disclosure:

Full-time IDEXX Employee

Hypoadrenocorticism FAQs

- Do we *have* to do an ACTH stim test to diagnose?
- How long do I have to stop glucocorticoids before ACTH stim test?
- ACTH stim results 'borderline' – post cortisol 3-5ish - now what?
- Is every dog an atypical Addisonian?
- What fluid do we use in an adrenal crisis?
- What dose of DOCP should I use?
- Does an addisonian with normal electrolytes need DOCP?
- Is hypoadrenocorticism a thing in cats?

**A disease by any other
name...**

ALIVE: Agreeing Language In Veterinary Endocrinology



Then and now...

Addison's disease

Atypical Addison's disease

Addisonian crisis

Relative adrenal insufficiency

Primary hypoadrenocorticism

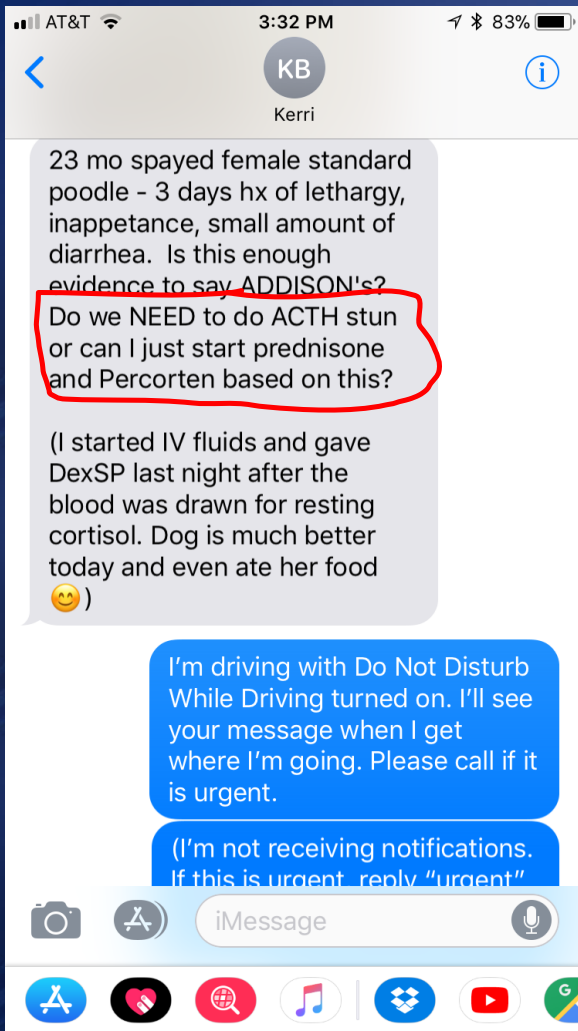
Eunatremic, eukalemic hypoadrenocorticism

Adrenal crisis

Critical illness-related corticosteroid insufficiency

Do we *have* to do an ACTH stimulation test to diagnose Addison's?

Yes.



Millie







When to perform ACTH stim test

- **Stable**
 - Off *all* glucocorticoids for ...
 - +/- Resting cortisol to screen
 - ACTH stim to confirm always
- **Shocky**
 - Stabilize prior to diagnostics
 - Use dexamethasone pending ACTH stim
 - Perform ACTH stim as soon as practical

**How long do I have to discontinue
glucocorticoids before ACTH stim test?**

If you're confused you're not alone...

Hypothalamic-pituitary-adrenal axis recovery after intermediate-acting glucocorticoid treatment in client-owned dogs

Francesca Del Baldo¹  | Andrea Corsini²  | Antonio Maria Tardo¹  |
Alessandro Tirolo¹ | Ada Sapignoli¹ | Michele Tumbarello¹ |
Kateryna Vasylyeva¹ | Federico Fracassi¹ 

- Treated with intermediate acting steroids for ≥ 7 days
- ACTH stim, eACTH stim 2-6d after d/c then q2 weeks until recover (post-stim cortisol >6 ug/dL)
- Median time to recovery: 3 days
- 11/20 at T0 (2-6 d)
- 6/20 at 2 weeks
- 2/20 required >8 weeks
- 1 dog at 4, 10, and 18 weeks!

Baseline cortisol can rule *out* Addison's

Baseline Cortisol

< 2 µg/dL is cutoff

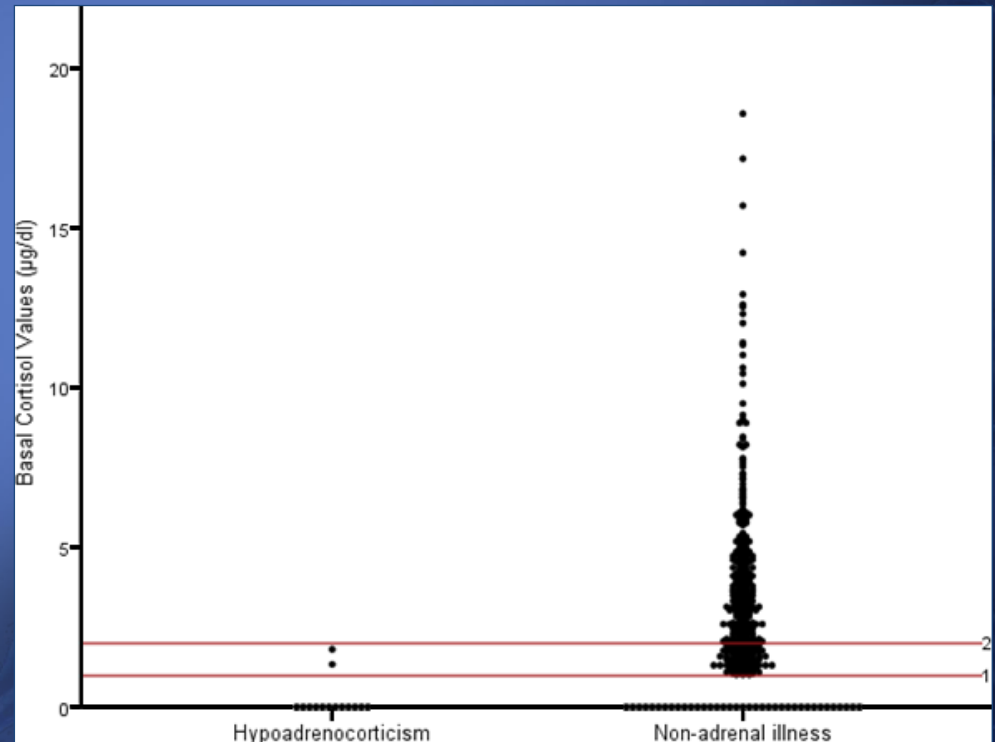
< 1 µg/dL increases
suspicion significantly

< 3 ug/dL not uncommon with primary
GI disease

Basal Serum Cortisol Concentration as a Screening Test for Hypoadrenocorticism in Dogs

C. Bovens, K. Tennant, J. Reeve, and K.F. Murphy

- 450 dogs, non-adrenal illness
 - (NOT ADDISON'S)
- 14 dogs, Addison's



| Number of Dogs with Hypoadrenocorticism | Basal Cortisol $\mu\text{g/dL}$ (nmol/L) | Cortisol after ACTH $\mu\text{g/dL}$ (nmol/L) |
|---|---|---|
| 12 | <1 (<28) | <1 (<28) |
| 1 | 1.33 (37) | 1.84 (51) |
| 1 | 1.80 (50) | 1.87 (52) |
| Reference interval | 1.80–9.0 (50–250) | 5.40–19.80 (150–550) |

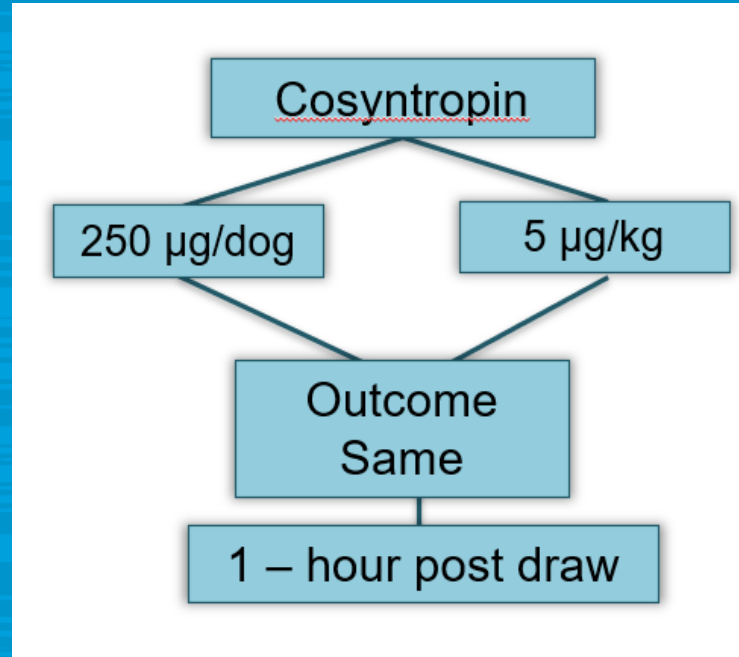
- $\leq 2 \mu\text{g/dL}$ rules out HOC

- 165 NAI dogs were $\leq 2 \mu\text{g/dL}$

- Baseline $\leq 2 \mu\text{g/dL}$


- Sensitivity: 100%
- Specificity: 63.3%
- **Prevalence 3%**
 - **PPV 7.8%**
 - **MANY FALSE POSITIVES**
- **Prevalence 15%**
 - **PPV 32%**

ACTH stimulation test



STANDARD ARTICLE

Low-dose ACTH stimulation testing in dogs suspected of hypoadrenocorticism

Annabel Botsford^{1,4} | Ellen N. Behrend¹  | Robert J. Kemppainen² | Philippe R. Gaillard³ | Frank Oprandy³ | Hollie P. Lee¹

- 1 µg/kg (µg/kg) cosyntropin, IV
 - (Can use up to 250 µg/dog)
 - NOT FOR CUSHING'S DIAGNOSIS!!!
- Reconstitute with 1 mL sterile saline
 - 250 µg/mL
- To make 10 µg/mL
 - Add 24 mL saline to 1 mL of 250 µg/mL
- 50 µg/mL
 - Add 4 mL saline to 1 mL of 250 µg/mL
- Store at -20° C (-4° F) for up to 6 months

What do I do with borderline stim results?

Post ACTH cortisol 3-5ish.

Call Dr. Lathan.

A retrospective study of dogs with atypical hypoadrenocorticism: a diagnostic cut-off or continuum?

J. A. WAKAYAMA¹, E. FURROW, L. K. MERKEL AND P. J. ARMSTRONG

- 9 dogs with stim results $> 2 \mu\text{g/dL}$ (3.4 – 8.1 $\mu\text{g/dL}$)
 - “Equivocal”
 - Follow-up median 24 months (10-77 months)
 - 2 dogs lost to follow-up
 - 3 dogs were clinically well after d/c’d pred
 - 4 dogs—no improvement with pred
 - **THESE DOGS DIDN’T HAVE ADDISON’S!!!**

Is every dog a possible atypical Addisonian?

Hmmm...

Aka glucocorticoid deficient hypoadrenocorticism and eunatremic eukalemic hypoadrenocorticism

RESEARCH

Open Access

Comparison between typical primary and eunatraemic, eukalaemic hypoadrenocorticism: 92 cases





Adrien Joaquim Da Silva^{1*}, Eilidh Gunn², Pedro Jose Guzmán Ramos³, Robert Edward Shiel³, Laura Bree⁴ and Carmel Therese Mooney¹

Prevalence and characterization of hypoadrenocorticism in dogs with signs of chronic gastrointestinal disease: A multicenter study

Christina Hauck¹  | Silke S. Schmitz²  | Iwan A. Burgener³  | Astrid Wehner¹ |
Reto Neiger⁴ | Barbara Kohn⁵ | Thomas Rieker⁶ | Sven Reese⁷ | Stefan Unterer¹

- Basal cortisol <2 µg/dL
 - 42/151 (28%) total dogs
 - 6/151 (6%) had Addison's
- Less common in another study
- UNCOMMON but life changing

Evaluation of resting cortisol concentration testing in dogs with chronic gastrointestinal signs

Ana Fernandez Gallego  | Adam G. Gow | Alisdair M. Boag 

- Basal cortisol $<2 \mu\text{g/dL}$
 - 79/282 (28%) total dogs
 - 1/282 had Addison's
- Repeat basal cortisol $>2\mu\text{g/dL}$ in 19/28
- Consider repeat basal cortisol testing prior to ACTH stim?

Suspect eunatremic, eukalemic hypoadrenocorticism when: (30-40%)

- **Gastrointestinal signs**
 - Megaesophagus?
- **Albumin:globulin <1.08**
 - Over 1/3 hyperglobulinemic
 - Hypoalbuminemia more common w EEH
- **Low cholesterol (<133 mg/dL)**
- **Lack of stress leukogram in sick animal**
 - Lymphocyte count >1500-1750cells/ μ L
 - Eosinophil count >500 cells/ μ L
- **Reticulocytosis without anemia**
- **Increasing Ca, decreasing BG, regurgitation...**

Formerly known as
Atypical Addison's.

Adrenal crisis: rethinking fluid choice

- LRS advantages
 - Contains buffer
 - Na concentration lower than 0.9% NaCl
 - Trivial K concentration
- 0.9% NaCl concerns
 - Higher Na concentration may raise serum Na too fast
 - Osmotic demyelination syndrome
 - Acidifying
 - Renal vasoconstriction due to high Cl concentration

Emergency treatment

- IV fluids
 - 10-15 ml/kg bolus over 15-30 min, reassess, repeat prn
- IV dexamethasone
 - 0.1-0.2 mg/kg IV then 0.05 mg/kg q12h for 24-72 h
 - No prednis(ol)one or hydrocortisone until ACTH stim completed
 - No advantage to hydrocortisone CRI v dexamethasone injections
- Dextrose if hypoglycemic
 - 1 gm/kg 50% dextrose diluted 1:4 then add 2.5-5.0% to fluids
- Blood products if severe anemia (GI bleed)

What dose of DOCP should I use?

Half of the traditional dose.

Maintenance treatment

- Prednisone
 - 0.1-0.2 mg/kg/day
 - **OFTEN LOWER**
 - 2-10X dose during stress or illness
- DOCP (deoxycorticosterone pivalate)
 - **1.1 mg/kg SQ/IM q28 days**
 - DOCP has no glucocorticoid activity – never sole treatment
- Monitor
 - Electrolytes at 14 days, then 28 days, eventually q3-6 months
 - CBC, biochemical panel, urinalysis at least yearly once stable
 - Lifelong

Does an Addisonian with normal lytes need DOCP?

Possibly...

Evaluation of Aldosterone Concentrations in Dogs with Hypoadrenocorticism

M.E. Baumstark, N.S. Sieber-Ruckstuhl, C. Müller, M. Wenger, F.S. Boretti, and C.E. Reusch

- 4/70 dogs with HA were atypical
 - 3/70: Na⁺ and K⁺ within reference range
 - 1/70: K⁺ decreased
 - ACTH-stimulated aldosterone undetectable in all
 - BUT do they need DOCP???
 - Measure aldosterone? Client/patient specific?
- 1 developed hyperkalemia 6 months later
- (Another study: Approx 10% will develop e-lyte abnormalities and require mineralocorticoid...)

Is hypoadrenocorticism a thing in cats?

Yes but rare.

Hypoadrenocorticism in cats: a 40-year update

Magdalena J Glebocka  and Alisdair Boag 

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1–7

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- 48 cases reported since 1983
- Autoimmune, lymphoma, trauma, congenital? (2 cats < 12 mo)
- Median age 4 yr, no breed or sex predilection
- Clinical signs and lab changes similar to dogs – lack of stress leukogram
- ACTH stim 5 ug/kg, 125 mcg/cat IV, IM, 30- and 60-min post samples
- Treatment similar to dogs but caution re volume overload

Clinical features and long-term management of cats with primary hypoadrenocorticism using desoxycorticosterone pivalate and prednisolone

Nadja S. Sieber-Ruckstuhl¹  | Livia Harburger¹ | Natalie Hofer¹ |
Claudia Kümmerle¹ | Claudia Müller¹ | Barbara Riond² |
Regina Hofmann-Lehmann² | Claudia E. Reusch¹ | Felicitas S. Boretti¹ 

Clinical findings, treatment, and outcomes in cats with naturally occurring hypoadrenocorticism: 41 cases

Emma Roberts¹  | Ian K. Ramsey²  | Ruth Gostelow³  | Anna Latysheva⁴ |
Luca Battaglia⁵ | Paolo Silvestrini⁶  | Ghita Benchekroun⁷  | Karen Brenner⁸ |
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Thank you!