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When Cushing's is Confusing and Addison's a Crisis.

Adrenal disease FAQs answered.

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IDEXX

Patty Lathan
Conflict of Interest Disclosure

I have financial interest, arrangement or affiliation with:

Name of Organization	Relationship
Idexx, Boehringer Ingelheim:	Consultant, honoraria
Merck Animal Health, Dechra Pharmaceuticals:	Honoraria

Bill Saxon

I have a direct or indirect relationship with IDEXX. Because of the nature of the relationship, it **will not** influence my presentation.

ASK YOUR ADDISON'S/ CUSHING'S QUESTIONS HERE!!!

Addison’s (Hypoadrenocorticism/ Adrenal Insufficiency)

PROJECT ALIVE: Agreeing Language In Veterinary Endocrinology

Hypoadrenocorticism FAQs

1. Do we *have* to do an ACTH stim test to diagnose Addison's?
2. ACTH stim results 'borderline' – post cortisol 3-5ish - now what?
3. Is every dog an atypical Addisonian?
4. What dose of DOCP should I use?
5. Does an addisonian with normal electrolytes need DOCP?

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

A: Yes.

Millie

AT&T 3:32 PM 83%

KB
Kerri

23 mo spayed female standard poodle - 3 days hx of lethargy, inappetance, small amount of diarrhea. Is this enough evidence to say ADDISON's? Do we NEED to do ACTH stun or can I just start prednisone and Percorten based on this?

(I started IV fluids and gave DexSP last night after the blood was drawn for resting cortisol. Dog is much better today and even ate her food 😊)

I'm driving with Do Not Disturb While Driving turned on. I'll see your message when I get where I'm going. Please call if it is urgent.

(I'm not receiving notifications. If this is urgent, reply "urgent"

iMessage

Baseline cortisol can rule *out* Addison's

Baseline Cortisol

- **< 2 µg/dL is the cutoff**
- **< 1 µg/dL increases suspicion significantly**
- **Not uncommon primary GI dogs to < 3 µg/dL**

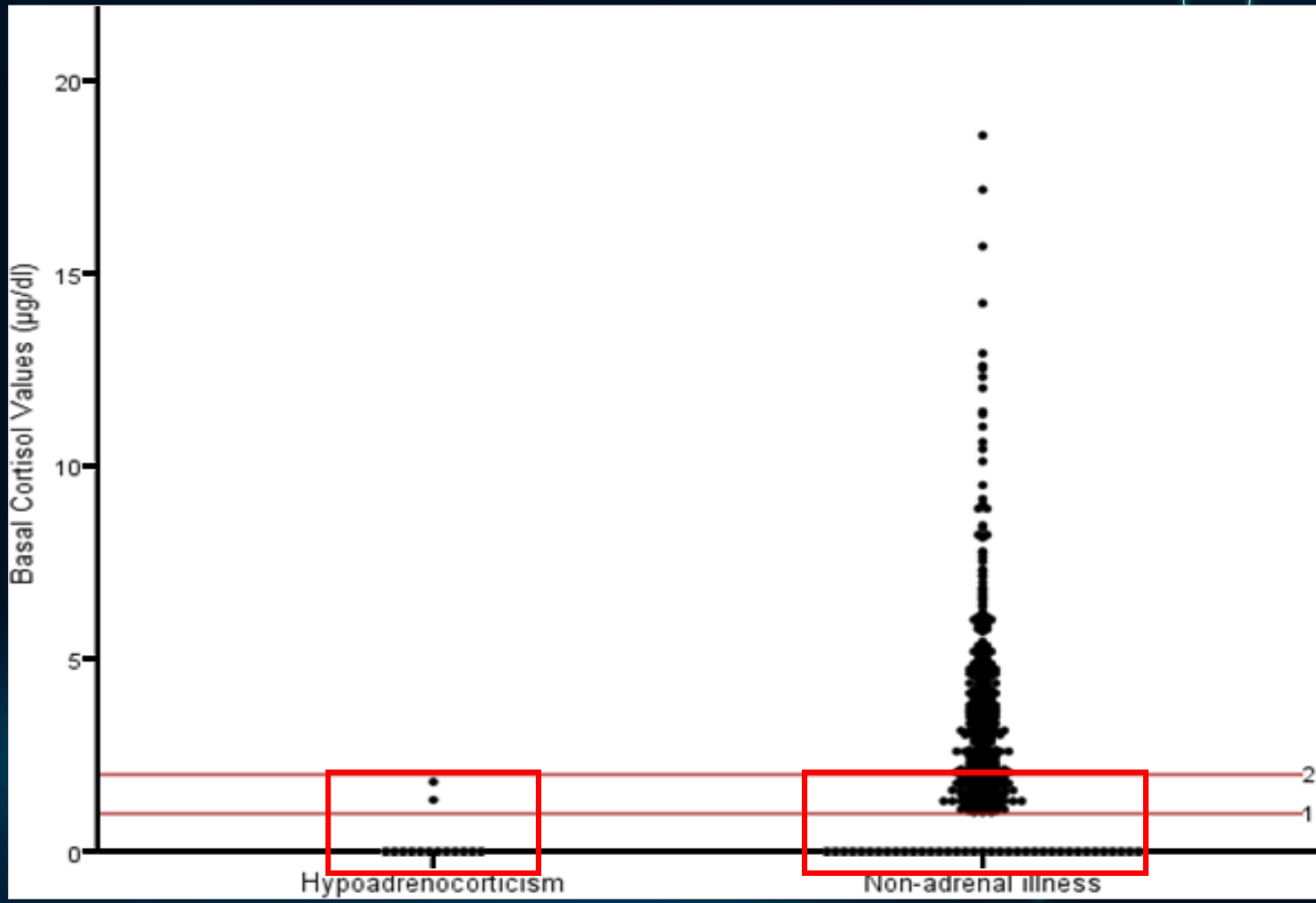
1. S.J. Ettinger, E.C. Feldman, .Hypoadrenocorticism. Textbook of Veterinary Internal Medicine..
2. Van Lanen K, Sande A. Canine hypoadrenocorticism: pathogenesis, diagnosis, and treatment. Top Companion Anim Med. 2014 Dec;29(4):88-95. doi: 10.1053/j.tcam.2014.10.001. Epub 2014 Oct 17. PMID: 25813848
3. Reagan, Krystle L., et al. "Characterization of clinicopathologic and abdominal ultrasound findings in dogs with glucocorticoid deficient hypoadrenocorticism." *Journal of Veterinary Internal Medicine* 36.6 (2022): 1947-1957..

J Vet Intern Med 2014;28:1541–1545

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

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

- All dogs with a stim over a 7 year period
- 450 dogs, non-adrenal illness
  - (NOT ADDISON'S)
- 14 dogs, Addison's

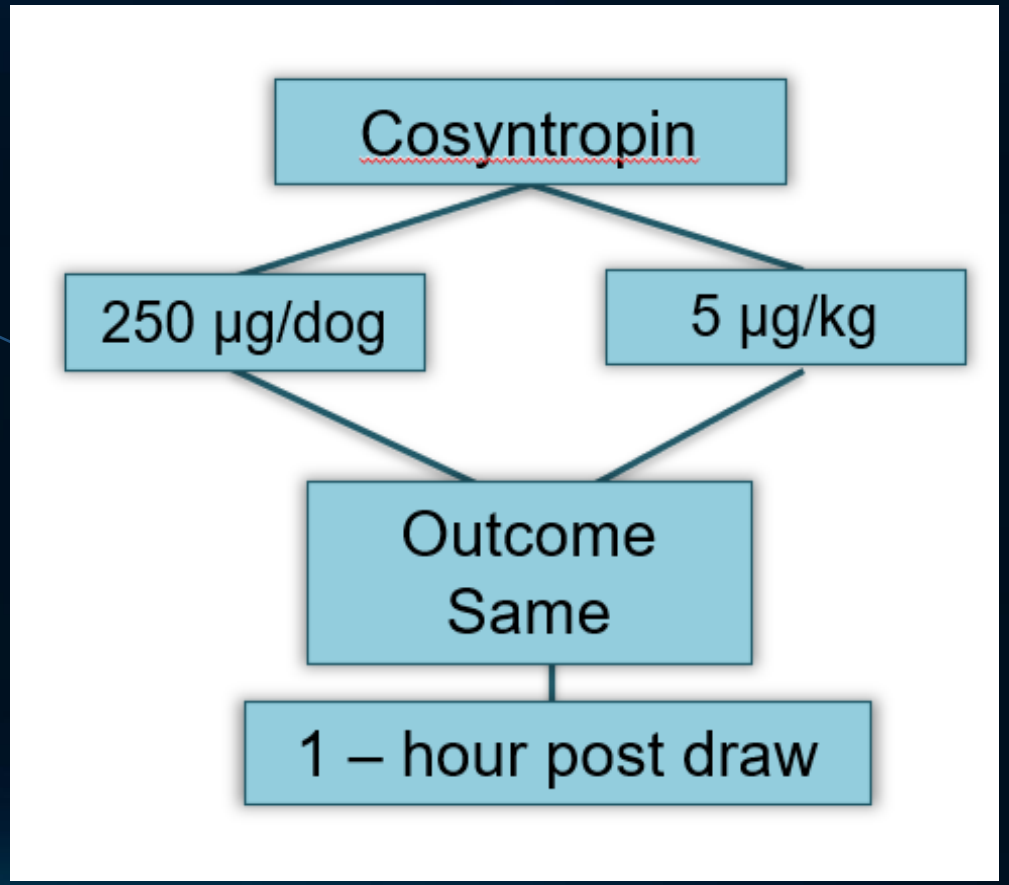


Number of Dogs with Hypoadrenocorticism	Basal Cortisol µg/dL (nmol/L)	Cortisol after ACTH µg/dL (nmol/L)
12	<1 (<28)	<1 (<28)
1	1.33 (37)	1.84 (51)
1	1.80 (50)	1.87 (52)
Reference interval	1.80–9.0 (50–250)	5.40–19.80 (150–550)

- ≥2 µg/dL rules out HOC
  - BUT…165 NAI dogs were ≤2 µg/dL

- Baseline ≤ 2 µg/dL
  - Sensitivity: 100%
  - Specificity: 63.3%
  - Prevalence 3%
    - PPV 7.8%
    - MANY FALSE POSITIVES
  - Prevalence 15%
    - PPV 32%

ACTH stimulation test



1. S.J. Ettinger, E.C. Feldman, .Hypoadrenocorticism. Textbook of Veterinary Internal Medicine..
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DOI: 10.1111/jvim.15256

Journal of Veterinary Internal Medicine Open Access

ACVIM American College of Veterinary Internal Medicine

STANDARD ARTICLE

Low-dose ACTH stimulation testing in dogs suspected of hypoadrenocorticism

Annabel Botsford[1,4] | Ellen N. Behrend[1] | Robert J. Kemppainen[2] | Philippe R. Gaillard[3] | Frank Oprandy[3] | Hollie P. Lee[1]

- 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

ASK YOUR ADDISON'S/ CUSHING'S QUESTIONS HERE!!!

Q: What do I do with borderline stim? (Post ACTH cortisol 3-5ish)

A: Call Dr. Lathan

PAPER

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

J. A. Wakayama[1], E. Furrow, L. K. Merkel and P. J. Armstrong

- 9 dogs with stim results > 2 µg/dL (3.4 – 8.1 µg/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!!!**

ASK YOUR ADDISON'S/ CUSHING'S QUESTIONS HERE!!!

Q: Is every dog a possible Atypical Addisonian?

A: Hmm…

STANDARD ARTICLE

Journal of Veterinary Internal Medicine Open Access

ACVIM American College of Veterinary Internal Medicine

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

Christina Hauck[1] | Silke S. Schmitz[2] | Iwan A. Burgener[3] | Astrid Wehner[1] | Reto Neiger[4] | Barbara Kohn[5] | Thomas Rieker[6] | Sven Reese[7] | Stefan Unterer[1]

- 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

Suspect eunatremic, eukalemic hypoadrenocorticism with:

(Disease formerly known as Atypical Addisons)

- Gastrointestinal signs (including melena!)
- Albumin:globulin <1.08
  - Over 1/3 hyperglobulinemic
- Low cholesterol (<133 mg/dL)
- Lack of stress leukogram in sick animal
  - Lymphocyte count >1500-1750cells/µL
  - Eosinophil count >500 cells/µL
- Hypoglycemia, megaesophagus, HL weakness…

Reagan KL, McLarty E, Marks SL, et.. al. Characterization of clinicopathologic and abdominal ultrasound findings in dogs with glucocorticoid deficient hypoadrenocorticism. J Vet Intern Med. 2022;36(6):1947-1957. doi:10.1111/jvim.16564

Addisonian crisis:

- Isotonic crystalloid
  - K content low
  - Safe
- 0.9% NaCl
  - Na content high
  - Maybe not safe
    - Osmotic demyelination syndrome
- 20-30 ml/kg IV, reassess, more prn

Q: What dose of DOCP should I use?

A: Half the traditional dose.

Treating Hypoadrenocorticism

- 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

Q: Does an Addisonian with normal lytes need DOCP?

A: Possibly.

J Vet Intern Med 2014;28:154–159

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…)

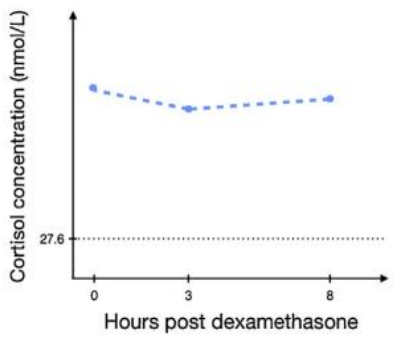
Cushing's Syndrome (Hyperadrenocorticism)

Cushing's Syndrome FAQs

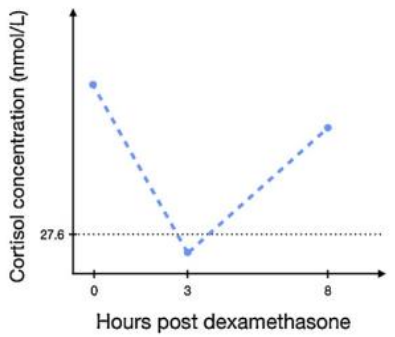
1. What's the best way to diagnose Cushing's?
2. My dog looks/acts cushingoid but the LDDST is normal, now what?
3. Does atypical Cushing's exist?
4. Do I have to differentiate between pituitary and adrenal disease?
5. What is the starting dose of trilostane?
6. Do we need an ACTH stim test to monitor therapy?

Q: What's the best way to diagnose Cushing's?

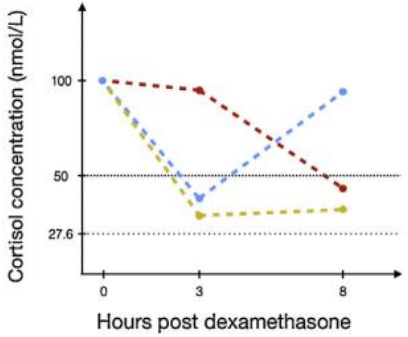
A: Right patient, LDDST, abdominal ultrasound.



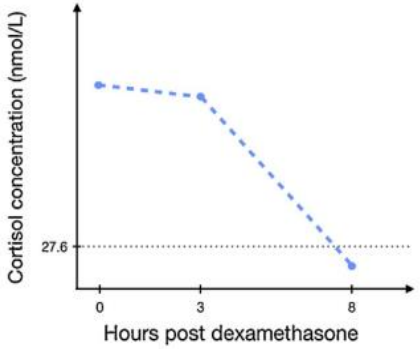
Lack of suppression



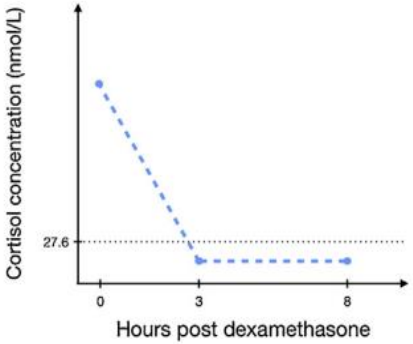
Escape



Partial suppression



Inverse



Complete suppression

Q: My dog looks/acts cushingoid but the LDDST is normal, now what?

A: 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 in 3-6 months if signs mild and no complications, e.g., hypertension, proteinuria….

Q: How far do I go to confirm ‘atypical Cushing’s?

A: Case by case it.

Atypical HAC 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

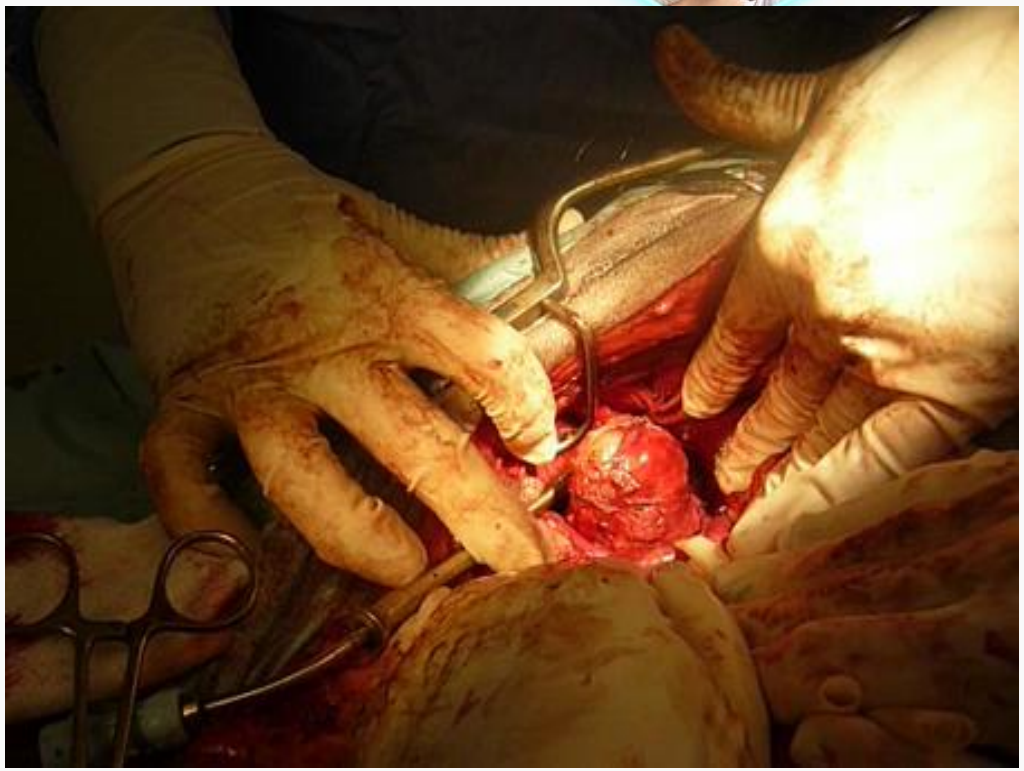
Q: Do I have to differentiate between pituitary and adrenal disease?

A: Yes please.

Differentiating PDH vs. AT 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



Q: What is the starting dose of trilostane?

A: We have the answer…

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

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

A: Mostly no.

Clinically Well, Controlled Dogs

(Useful picture slide)

- **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!