



Addison's Disease "The Great Pretender"



Wendy Blount, DVM


Are You Missing Addison's?

- The average vet in private practice sees 1500 dogs per year
- Addison's Disease occurs in 0.5 dogs per thousand
- Solo practice vet should diagnose one new case every other year
- If untreated, Addison's can be fatal
- Severity varies
- If treated, prognosis is excellent
- Median survival 7 years with treatment




Are You Missing Addison's?

- What about cats?
- Addison's is exceedingly rare in cats
- There are less than 10 in the published literature that I can find
- If you diagnose a cat with Addison's make sure you are adapting your ACTH stim test to the cat
- Post ACTH samples at 30 & 60 minutes



What Does Addison's Look Like?



- Breed
 - "Mixed" is the most common breed
 - Genetic predisposition in
 - Standard Poodle***
 - Portuguese Water Dog
 - Bearded Collie
 - Labrador Retriever
 - Pointer



What Does Addison's Look Like?

Dot

- 2-1/2 year old SF Peke-a-Poo
- **CC** - She has no energy and does not eat well
- Sometimes she acts like she's dead
- **Exam** – BCS 4/9, dull mentation


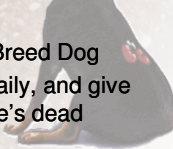



What Does Addison's Look Like?

Dot

- **CBC** - normal
- **Panel** – glucose 52 mg/dl
- **Urinalysis** – SG 1.023
- **Electrolytes** – normal

Diagnosis - Hypoglycemia of Toy Breed Dog
Treatment - Multiple small meals daily, and give Karo syrup when she acts like she's dead

What Does Addison's Look Like?

Dot

- Episodes continue with only mild response to therapy
- **Exam** – BCS 3/9, poor muscle tone, dull mentation
- **DDx stubborn hypoglycemia**
 - Liver disease
 - Insulinoma
 - Occult infection/sepsis
 - Addison's Disease
 - (Glucagon deficiency, Polycythemia)



What Does Addison's Look Like?

Dot

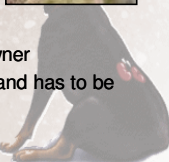
- **Bile Acids**
 - normal fasting and 2 hrs post meal
- **Insulin and glucose levels**
 - normal
- **Chest x-rays and abdominal US**
 - normal
- **ACTH stimulation test**
 - Pre-ACTH – 0.2 ug/dl
 - Post-ACTH – 0.8 ug/dl



What Does Addison's Look Like?

Dot

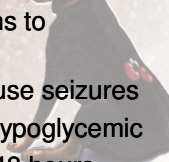
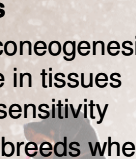
- **Tx** – Percorten q28 days
- **1 year follow-up**
 - Dot eats like a pig and feels better than she has in her whole life
 - BCS increases to 6/9 in 6 weeks
 - Playful and “full of it” according to owner
 - Dot is no longer a compliant patient and has to be muzzled for her Percorten shot
 - I liked Dot better before



What Does Addison's Look Like?

Hypoglycemia and Addison's

- Glucocorticoids increase gluconeogenesis while decreasing glucose use in tissues via increase insulin receptor sensitivity
- May be more common in toy breeds where there are other predispositions to hypoglycemia
- Can be severe enough to cause seizures
- 20-25% of Addisonians are hypoglycemic
- Responds the therapy in 24-48 hours



What Does Addison's Look Like?

Jovi

- 1-1/2 year old SF Great Dane
- 120 lbs
- **CC** – Referred for chronic cough vomiting
- Not eating for 2 days
- **Exam** – BCS 4/6, temp 104F



What Does Addison's Look Like?

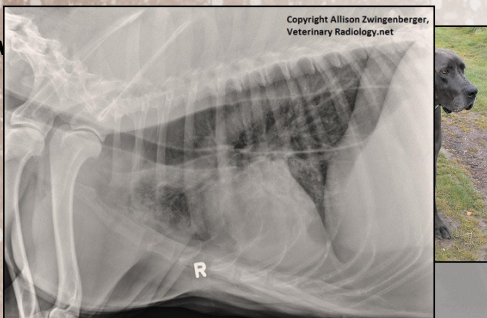
Jovi

- **CBC**
 - PCV 30%
 - Neutrophils 38,000/ul
 - Monocytes 2,700/ul
- **panel** – albumin 2.2 g/dl
- **UA** – no abnormalities
- **Electrolytes/blood gases** - normal
- **Thoracic radiographs**



What Does Addison's Look Like?

Jovi




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What Does Addison's Look Like?

Jovi


- **DDx Megaesophagus**
 - Idiopathic
 - (Obstruction
 - Vascular ring anomaly
 - Stricture)
 - Hypothyroidism
 - Hypoadrenocorticism
 - Myasthenia gravis
 - Esophagitis



What Does Addison's Look Like?

Jovi


- **Thyroid Panel**
 - TSH - undetectable
 - TT4 – 2.9 (low)
 - fT4 - normal
- **ACTH Stimulation Test**
 - Pre ACTH cortisol – 0 ug/dl
 - Post ACTH cortisol – 0 ug/dl
- **Anti Ach Receptor Antibody**
 - negative



What Does Addison's Look Like?

Jovi


- **Dx**
 - Megaesophagus due to hypoadrenocorticism
 - Secondary aspiration pneumonia
 - Sick euthyroid



What Does Addison's Look Like?


Jovi

- **Tx**
 - Prednisone 10 mg PO SID
 - Amoxicillin 1500 mg PO BID x 4-8 weeks
 - Ciprofloxacin 500 mg PO BID x 4-8 weeks
 - Follow pneumonia with chest x-rays
 - Jovi eventually needed treatment also with mineralocorticoids
 - Megaesophagus due to Addison's responds well to treatment



What Does Addison's Look Like?

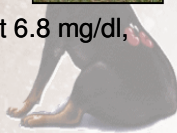
- **Hypoalbuminemia and Addison's**
 - Albumin may have been contributed to also by lung infection in this case
 - Hypoalbuminemia can be the primary presenting symptom of Addison's



What Does Addison's Look Like?

LuLu

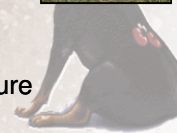
- 6 year old SF Blue Heeler
- **CC** – referred for ICU care for acute renal failure
- **CBC** – PCV 32%
- **Panel** - BUN 255 mg/dl, creat 6.8 mg/dl, phos 10.9 mg/dl
- **UA** – SG 1.016



What Does Addison's Look Like?

LuLu

- **Electrolytes/blood gases**
 - K 5.9 mEq/L
 - Na 145 mEq/L
 - pH venous 7.293
 - TCO2 16 mEq/L
- **Abdominal US** – normal
- **Dx** – acute oliguric renal failure



What Does Addison's Look Like?

LuLu

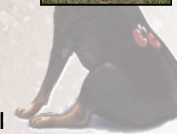
- **DDx**
 - Pyelonephritis
 - Leptospirosis
 - Toxicity
- Responded beautifully to treatment
 - IV fluid therapy x 5 days
 - Aluminum hydroxide PO
 - Ampicillin IV TID



What Does Addison's Look Like?

LuLu

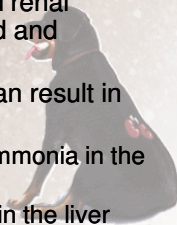
- **Lulu returned in 10 days**
 - Similar presentation
- **DDx**
 - Chronic renal failure
 - hypoadrenocorticism
- **ACTH stimulation test**
 - Pre ACTH cortisol – 1.1 ug/dl
 - Post ACTH cortisol – 1.5 ug/dl



What Does Addison's Look Like?

Azotemia and Addison's

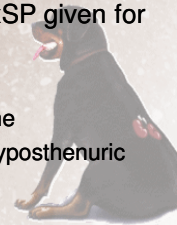
- Hypovolemia causing decreased renal perfusion and prerenal azotemia
- Can result in renal injury and renal azotemia if severe, prolonged and untreated
- Hemorrhage in the GI tract can result in increased BUN
 - GI bleeding leads to more ammonia in the colon
 - Ammonia converted to urea in the liver



What Does Addison's Look Like?

Azotemia and Addison's

- If no renal injury, azotemia responds quickly to fluid therapy
- Responds even better if DexSP given for shock
- Urine specific gravity
 - Often mildly concentrated urine
 - Can also be isosthenuric or hyposthenuric due to medullary washout



What Does Addison's Look Like?

Doc

- 3 year old CM Standard Poodle
- **CC** – vomiting, weight loss, drinking massive amts of water, anorexia
- **CBC** – PCV 28%
- **Panel** – calcium 15 mg/dl (not lipemic)
- **UA** – SG 1.005
- **Urine culture** – negative



What Does Addison's Look Like?

Doc

- **DDx hypercalcemia**
 - Malignancy
 - Primary hyperparathyroidism
 - Renal disease
 - Granulomatous inflammation
 - Hypervitaminosis D
- **Rectal exam** - normal
- **Chest x-rays and abdominal US** – normal



What Does Addison's Look Like?

Doc

- **PTH** – low
- **Ionized calcium** – high
- **PTHrP** – negative
- **ACTH stimulation**
 - Pre ACTH cortisol – 0.8 ug/dl
 - Post ACTH cortisol – 1.1 ug/dl



What Does Addison's Look Like?

PU-PD and Addison's

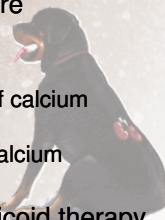
- Excessive sodium loss into the urine causes medullary washout.
- Hypercalcemia can also contribute, if present



What Does Addison's Look Like?

Hypercalcemia and Addison's

- More likely in Addisonians with more severe disease and hyperkalemia
- 29% of primary Addisonians are hypercalcemic
- Mechanism – unsure
 - Possible hemoconcentrations of calcium binding serum proteins
 - Decreased renal clearance of calcium
 - Cortisol antagonizes vitamin D
- Responds rapidly to glucocorticoid therapy



What Does Addison's Look Like?

Chevy

- 9 year old 12 lb SF Rat Terrier
- **CC** – taken to out-of-town vet 5 days ago after having vomiting and diarrhea on summer vacation
- **Tx**
 - SC fluids
 - DepoMedrol 1cc
 - Rimadyl x 7 days
- Felt better for 24 hours, but now feels really bad, won't eat and has "unbelievably foul diarrhea"



What Does Addison's Look Like?

Chevy

• Exam

- dehydrated 8%
- pale mucous membranes
- weak pulses
- projectile stools resembling a range between raspberry jam to beach tar or some mixture thereof
- HR 86 beats per minute
- temp 97.1F
- Abdominal pain on palpation



What Does Addison's Look Like?

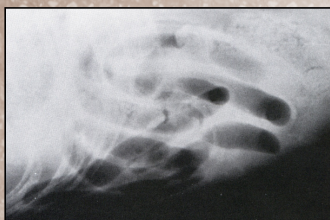
Chevy

- **CBC** – PCV 35%
- **Panel**
 - BUN 68 mg/dl, creat 2.4 mg/dl
 - albumin 2.1 g/dl
 - SAP 1100 U/L
- **Electrolytes** – K 6.8 mEq/L, Na 142 mEq/L
- **UA** – SG 1.022
- **PT/PTT** - normal
- **Abdominal radiographs & ECG**



What Does Addison's Look Like?

Chevy



What Does Addison's Look Like?

Chevy

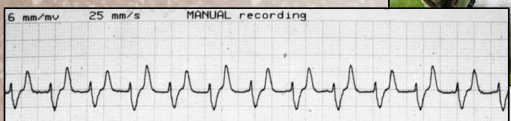


- **No distinct P waves**
 - **Tall spiked T waves**
 - **QRS relatively normal**
- Bradycardia likely due to hyperkalemia**

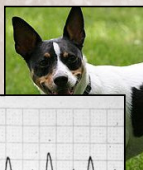


What Does Addison's Look Like?

Chevy



- **A more severe hyperkalemia ECG from a blocked tomcat with potassium 9.2 mEq/L**



What Does Addison's Look Like?

Chevy

- **DDx – ileus, GI hemorrhage, abdominal pain and shock**
 - GI foreign body
 - GI ulceration ± perforation
 - NSAID + DepoMedrol toxicity
 - Hemorrhagic gastroenteritis (HGE)
 - Anaphylaxis
 - Sepsis
 - Addison's Disease



What Does Addison's Look Like?

Chevy

• Plan

- Diagnostic
 - abdominal US
 - \pm barium study
 - No endoscope immediately available
- Therapeutic
 - IV fluids
 - ampicillin/enrofloxacin IV
 - Possible diagnostic surgery if perforation or foreign body is suspected



What Does Addison's Look Like?

Chevy

• DDx Azotemia with whimpy urine concentration

- Dehydration/hypovolemia**
- GI hemorrhage**
- Sepsis**
- Pyelonephritis
- Addison's Disease
- (Early acute renal failure)



What Does Addison's Look Like?

Chevy

• DDx hyperkalemia

- Severe GI disease
- sepsis
- Addison's Disease
- acidosis
- (Early acute renal failure)
- **Mild to moderate hypoalbuminemia and increased SAP could be explained by the GI hemorrhage**



What Does Addison's Look Like?

Chevy

• Abdominal US

- No free fluid in the abdomen suggesting perforation
- No apparent foreign body
- No severe ulcer
- No abnormalities, but careful interrogation was difficult due to excess gas in the gut
- **Barium study** – motility slow, but no obstruction and no filling defects



What Does Addison's Look Like?

Chevy

- Chevy remarkable better the next day and eating in 48 hours
- Diarrhea improved and resolved over 3-4 days
- **Tx**
 - Amoxicillin BID x 10 days
 - Carafate TID x 5 days
 - Discuss Addison's Disease with the owner



What Does Addison's Look Like?

Chevy

- Chevy did well for one month, then GI signs returned
 - Anorexia, vomiting, diarrhea
- **ACTH stim**
 - Pre ACTH cortisol 1.4 ug/dl
 - Post ACTH cortisol 1.9 ug/dl
- 4 years later, Chevy is doing very well on Percorten therapy



What Does Addison's Look Like?

Kelsey

- 8 month old SF Rottweiler
 - Owned by a vet student
- **CC** - muscle tremors in the right front leg
- **CBC** – lymphocytes 6,000/uI
- **Panel/UA** – normal
- **Electrolytes** – Na 140 mEq/L, K 5.7 mEq/L
- **ACTH stim** – baseline 1.7, post ACTH 2.0



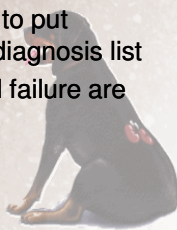
What Does Addison's Look Like?

- Addison's Disease can have many, many different presentations
- Suspicion of Addison's can be confirmed only when Addison's is on the differential diagnosis list
- ACTH stim for Addison's is a simple test that is easy to perform and interpret
- **The difficulty in diagnosing Addison's is not in performing complicated diagnostics, but in actually considering it as a possibility**

What Does Addison's Look Like?

Blood Pressure and Addison's

- 90% of people with untreated Addison's Disease are hypotensive
- Hypotension can remind you to put Addison's on the differential diagnosis list
- Many dogs with chronic renal failure are hypertensive



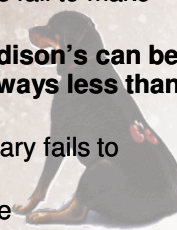
ACTH Stimulation Test

Post value <2 ug/dl confirms primary Addison's Disease

- Primary Addison's = adrenals fail to make cortisol and/or aldosterone

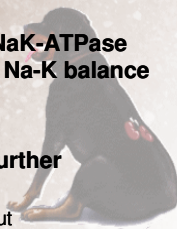
Post value on secondary Addison's can be as high as 3-4 ug/dl, but always less than 5 ug/dl

- Secondary Addison's = pituitary fails to make ACTH
- These are harder to diagnose



Na:K Ratio

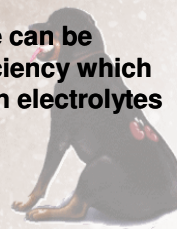
- **Aldosterone deficiency (mineralocorticoid) makes it impossible for the kidneys to conserve sodium or excrete potassium properly**
- **Cortisol deficiency precludes NaK-ATPase pump from maintaining proper Na-K balance**
 - Intracellular potassium decreases
 - Intracellular sodium increases
- **Acidosis due to hypovolemia further exacerbates Na-K imbalance**
 - As H⁺ moves into cells, K⁺ moves out



Na:K Ratio

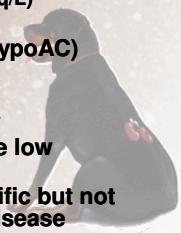
However....

- Dehydration can mask hyponatremia and hypochloremia
- Adrenal Addison's disease can be purely glucocorticoid deficiency which has a less marked effect on electrolytes
 - Abnormalities can be subtle




Na:K Ratio

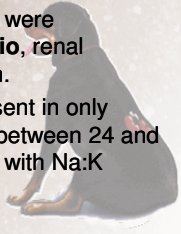
Thumb Rules

- **Adrenal (primary) Addison's**
 - 86% have hyponatremia (<142 mEq/L)
 - 95% have hyperkalemia (>5.5 mEq/L)
 - 4% have normal K, Na and Cl
 - **ACTH deficiency (secondary HypoAC)**
 - 35% have hyponatremia
 - Unlikely to cause hyperkalemia
 - Clinical glucocorticoid deficiency
 - **Addisonians almost never have low potassium or high sodium**
 - **Decreased Na:K is highly specific but not sensitive at all for Addison's disease**
- 

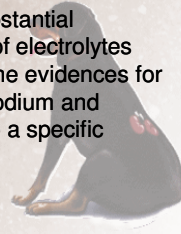
Na:K Ratio

- **Mike Willard was amongst the earliest veterinary authors to embrace Na:K <27-28 as a diagnostic method for Addison's**
 - **Mike Willard, 2005 – personal conversation**
 - “I wish I had never written that paper”
- 

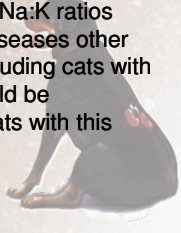
Na:K Ratio

- **Roth et al 1999, J Vet Diagn Invest**
 - **Evaluation of low sodium:potassium ratios in dogs.**
 - Although numerous conditions were associated with a low Na:K **ratio**, renal disease was the most common.
 - Hypoadrenocorticism was present in only 13% of **dogs** with Na:K ratios between 24 and 15 but was present in all **dogs** with Na:K ratios <15.
- 

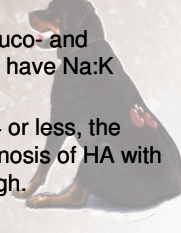
Na:K Ratio

- **Pak 2000, J Vet Science**
 - **The clinical implication of sodium-potassium ratios in dogs.**
 - Although there have been substantial evidences on the usefulness of electrolytes for the diagnosis of disease, the evidences for a direct link between serum sodium and serum potassium in relation to a specific disease are very limited.
- 

Na:K Ratio

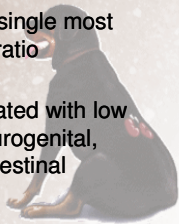
- **Willard 2005, Vet Clin Path**
 - **Decreased sodium:potassium ratios in cats: 49 cases**
 - “CONCLUSIONS: Decreased Na:K ratios frequently occur in cats with diseases other than hypoadrenocorticism, including cats with effusions. These findings should be considered when evaluating cats with this biochemical abnormality.”
- 

Na:K Ratio

- **Adler et al. JAVIM 2007**
 - **Abnormalities of serum electrolyte concentrations in dogs with hypoadrenocorticism.**
 - Most Addisonians with both gluco- and mineralocorticoid insufficiency have Na:K ratios of 27-28 or less.
 - In dogs with a Na:K ratio of 24 or less, the likelihood of confirming a diagnosis of HA with an ACTH stimulation test is high.
- 

Na:K Ratio

- **Neilsen et al, Vet Record 2008**
 - Low ratios of sodium to potassium in the serum of 238 dogs.
 - Hypoadrenocorticism was the single most common cause of a low Na:K ratio
 - 27 (16.7%) of the cases.
 - Other clinical problems associated with low Na:K ratios included different urogenital, cardiorespiratory and gastrointestinal diseases (83.3%).



Na:K Ratio

Conclusions

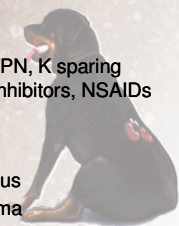
- There are many causes of Na:K < 27-28
 - Only 15-17% of these are Addisonian
- Other causes include:
 - Abdominal or thoracic effusion
 - Cardiorespiratory disease
 - Acidosis
 - Trauma or reperfusion injury
 - Sepsis
 - Diabetic Ketoacidosis
 - Uremia (oliguric renal failure, obstruction/rupture)



Na:K Ratio

Conclusions

- Other causes include:
 - Liver failure
 - Toxicity
 - Mushrooms, IV fluid therapy or TPN, K sparing diuretics (spironolactone), ACE inhibitors, NSAIDs
 - Artifacts
 - Extreme leukocytosis
 - Hemolysis in Akitas and Shiba inus
 - Running serology on EDTA plasma



Na:K Ratio

Conclusions

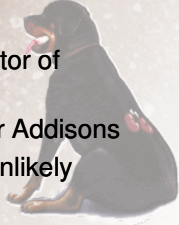
- Other causes include:
 - GI disease
 - Whipworms, hookworms
 - Pancreatitis
 - GDV
 - ulcers, especially if perforation
 - Canine parvovirus
 - Canine distemper virus
 - severe malabsorption**
 - Severe deep pyoderma



Na:K Ratio

Conclusions – The Bottom Line

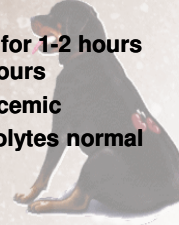
- Most Addisonians that lack both gluco- and mineralocorticoid deficiencies have Na:K <27
- Na:K <24 is a stronger indicator of hypoAC
- Na:K <15 is even stronger for Addisons
- Na:K >28 makes Addison's unlikely



Treatment of the Crisis

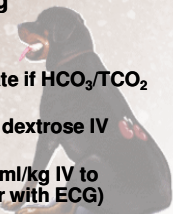
• Correct hypotension

- Death due to hypoadrenocorticism is usually due to vascular collapse (not hyperkalemia)
- 0.9% NaCl at 40-80 ml/kg/hr for 1-2 hours then 1-2 ml/lb/hr for 36-48 hours
- Add 5% dextrose if hypoglycemic
- Change to LRS when electrolytes normal and BP returns to normal



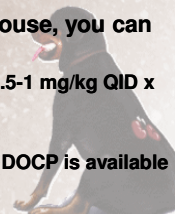
Treatment of the Crisis

- Dexamethasone 0.5-2 mg/kg initial
 - Then 0.01-0.05 mg/kg daily until prednisone can be given PO
- If K > 8 mEq/L, consider treating hyperkalemia
 - Rarely necessary after 1 hr fluids
 - then treat acidosis with bicarbonate if $\text{HCO}_3/\text{TCO}_2$ still <12
 - Then 0.3-0.5 U/10 lbs insulin + 5% dextrose IV fluids
 - Or Calcium gluconate 10% - 0.5-1 ml/kg IV to effect over 10-20 minutes (monitor with ECG)



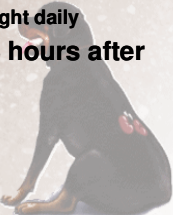
Treatment of the Crisis

- Start mineralocorticoid
 - DOCP 1 mg/lb IM q25-30 days
 - Respond within 6-8 hours
 - If you don't have DOCP in house, you can use hydrocortisone IV:
 - 1.25 mg/kg initial dose, then 0.5-1 mg/kg QID x doses
 - Then 0.1-0.25 mg/kg QID
 - Then 0.1-0.25 mg/kg BID until DOCP is available
 - Not as effective as DOCP



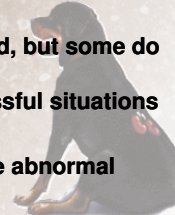
Treatment of the Crisis

- Start mineralocorticoid
 - Or fludrocortisone
 - Oral therapy doesn't work well if vomiting
 - 1.5-2 tablets per 5 lbs body weight daily
- Close observation for 24-48 hours after stopping IV fluids



Chronic Therapy

- DOCP 1 mg/lb IM q25-28 days
- Prednisone 0.1 mg/lb/day PO, and wean down to the lowest effective dose
 - Often every other day
 - Texts say all dogs need pred, but some do well on DOCP only
 - Keep pred on hand for stressful situations
- Recheck in 2 weeks
 - BUN, glucose, anything else abnormal
 - electrolytes



Chronic Therapy

- Recheck electrolytes in 30 days
 - Sooner if not well
- Recheck electrolytes once monthly for 3-6 months
 - Sooner if not well
- Then every 3-6 months
- CBC, panel, UA q6 months



Desoxycorticosterone Pivalate (DOCP)

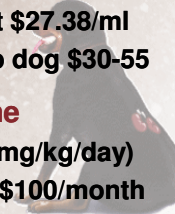
Percorten®

Zycortal®

- | | |
|---------------------|---------------------|
| • Elanco | • Dechra |
| • 25 mg/ml | • 25 mg/ml |
| • Cost \$38.69/ml | • Cost \$27.38/ml |
| • 50 lb dog \$40-80 | • 50 lb dog \$30-55 |

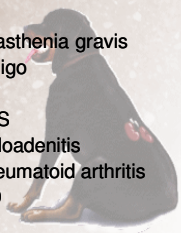
Fludrocortisone

- 0.1 mg/tab, generic (0.02 mg/kg/day)
- Cost \$0.75/tab, 50 lb dog \$100/month



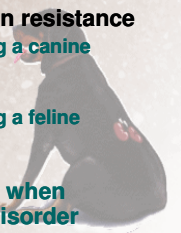
Polyendocrine Syndrome

- Also called “Schmidt’s Syndrome” in people
- Caused by LP inflammation in more than one endocrine gland, causing failure of at least 2 glands
- The 2nd endocrinopathy develops 6 months to 2 years after the first
 - Parathyroid
 - Myasthenia gravis
 - Adrenal
 - Vitiligo
 - Gonads
 - ITP
 - Thyroid
 - KCS
 - Pancreas - DM
 - Sialoadenitis
 - Pituitary - DI
 - Rheumatoid arthritis
 - IBD




Polyendocrine Syndrome

- Most commonly affected glands
 - Thyroid
 - Pancreas
 - Adrenal
- Abnormal T4 can result in insulin resistance
 - If you are having trouble regulating a canine diabetic, look for hypothyroidism
 - Check TSH, T4, freeT4
 - If you are having trouble regulating a feline diabetic, look for hyperthyroidism
 - Check T4, freeT4
- Be ready to reduce insulin dose when initiating treatment for thyroid disorder




Polyendocrine Syndrome


- Thyroid hormones facilitate cortisol clearance
- Dogs with untreated hypothyroidism AND untreated Addison’s disease will have conservation of cortisol levels due to lack of thyroid hormones
- So they may not show signs of Addison’s
- Treatment of the hypothyroid state can cause precipitation of an Addisonian Crisis
- If a hypothyroid dog crashes when you treat it, do an ACTH stim



In a Nutshell




[link](#)




Summary

- [PowerPoint Handout](#) goes behind the yellow tab (Cushing's PPT → blue sheet → Addison's PPT)
- **Vet Handouts**
 - [Adrenal Testing Summary](#)
 - [Bicarbonate Administration](#)
- **Client Handouts**
 - [Hypoadrenocorticism](#)
 - [Polyendocrine Failure](#)



Summary

- **Drug Handouts**
 - [DOCP](#)
 - [Fludrocortisone](#)
 - [Prednisone](#)



Acknowledgements

J Catharine Scott-Moncrief. Canine & Feline
Endocrinology, 4th Edition. Ch 12 – Canine
Hypoadrenocorticism.

