Hyperadrenocorticism

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HAC - Two Types
PDH - Pituitary Dependent Hyperadrenocorticism
• 80-85%
ADH - Adrenal Dependent Hyperadrenocorticism
• 15-20%

Signalment

#1 Dog Breed for Cushing’s and Addison’s
• Poodle

Age
• 75% of dogs with PDH are > 9 years
• 90% of dogs with ADH are > 9 years
• HAC in dogs < 2yrs old is exceedingly rare
• Feline HAC has wider variation in age

Clinical Signs – Common
Both Dog and Cat
• PU-PD
• Inc Liver Enzymes
  – Dogs > Cats
• Hepatomegaly
  • Pot bellied
• Muscle wasting
• Polyphagia
• Hypertension
• Urinary Tract Infection
  • 20%
• Skin Changes
  – Skin fragility - cats > dogs
  – Excessive bruising
  – Endocrine alopecia
  – Pyoderma
  – Fat pads on the neck

Clinical Signs – Common
Dogs
• STissue Calcification
• Respiratory Syndrome
• Feminization of males
• Virilization of females
• Stress Leukogram
• Hyperpigmentation
• Secondary Hypothyroid
• Weight Gain
• Hyperlipidemia

Cats
• Diabetes Mellitus
  • 75-85% cats; 5% dogs
• Weight Loss
• Diarrhea, Vomiting
• Poor Grooming
• Acromegaly
• Stress Leukogram
• Hyperthyroid
• Hyperparathyroidism
• Hyperlipidemia

Clinical Signs – Common
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• Stress Leukogram
• Hyperthyroid
• Hyperparathyroidism
• Hyperlipidemia
Clinical Signs - Rare

**Dogs**
- Hemoabdomen
- Cerebral Neuro Signs
  - 10%
- Facial paralysis
- Joint Laxity
- Ruptured Cruciate
- Sudden Blindness
- Exophthalmos
- CaOxalate Uroliths

**Both**
- Demodex
- Plantigrade stance

**Cats**
- Palpable adrenal mass

Clinical Signs - Clues

Severe hepatomegaly with few signs of liver failure – think HAC or neoplasia
- Bile acids normal (mildly elevated 30%)
- Albumin normal

Concentrated urine
- Can't possibly be PU-PD
- HAC very unlikely, unless has been water deprived

Bacteriuria without inflammatory sediment
- Consistent with UTI in an immunocompromised animal
- Rarely any lower urinary tract signs with UTI (50%)

Respiratory Syndrome

- Panting
- Coughing
- Cyanosis
- Polycythemia

Pulmonary thromboembolism is a common feature of the syndrome

Collapsing trachea is a common concurrent disease

Renal Disease and HAC

Some recommend against treating HAC when there is concurrent CRF
- PU-PD can keep CRF compensated
- Treating HAC can unmask anorexia due to CRF
- Increased cortisol levels can improve general well being, despite significant underlying illness
- Treat HAC only if severe and life threatening
- Rule out pyelonephritis as a cause of apparent renal disease
- Eliminate pyelonephritis prior to beginning therapy for HAC

SARDS and HAC

SARDS
- Sudden Acquired Retinal Degeneration Syndrome

Adrenal Tests Look Cushingoid

Apparent HAC rarely needs treatment

Usually resolves on its own

Schnauzers

Clues on the Radiographs

**Abdominal Films**
- Hepatomegaly
- Good contrast due to abdominal fat
- Distended urinary bladder
- 50% of adrenal masses are mineralized (5-10% of HAC)
- Uncalcified tumors < 2 cm won’t be seen
- Calcinosi cutis, other mineralized soft tissue
- Osteopenia (rare)
Clues on the Radiographs

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Clues on the Radiographs

Thoracic Films
• Signs of PTE
  - Hypovascular areas acutely
  - Alveolar infiltrates due to atelectasis, hemorrhage, infarction
  - Interstitial infiltrates (soft tissue density)
  - Enlarged pulmonary arteries
  - Right sided heart enlargement
  - Mild pleural effusion

Clues on the Radiographs

Thoracic Films
• Mineralized airways
• Interstitial lung pattern
• Metastasis if malignant ADH
• Osteopenia (rare)

Diagnosis

Screening Tests
• Urine creatinine:cortisol
• ACTH Stimulation Test
• Low Dose Dexamethasone Test
• Combined ACTH stim - LDD

Differentiating Tests
• Abdominal Ultrasound
• Atypical ACTH stim
• (Endogenous ACTH)
• (High Dexamethasone Test - HDD)

Diagnosis

Monitoring Tests
• Baseline Cortisol
• ACTH Stimulation Test
• Electrolytes, kidney panel
Diagnosis

Cortisol Assay Samples
- EDTA-plasma, serum or urine
- Centrifuge ASAP
- Plasma will give you greater volume
- Be consistent with each patient (all samples plasma, or all samples serum)
- Ship on ice packs for delivery in 1-2 days

Urine creatinine:cortisol (UCC)
- A good screening test
- Negative (normal) result rules out HAC
- Positive (increased) result tells you the dog is sick
- 76% of dogs with non-adrenal illness have elevated UCC
- Have owner collect urine at home to eliminate stress (non-absorbent litter for cats)
- Not a reliable for monitoring therapy
- Little data available on reliability in cats
  - UCC 3x higher in hospitalized cats relative to home
  - Sick cats have UCC much higher than well cats

ACTH Stimulation Test

Tests the capacity of the adrenal gland to secrete cortisol

Advantages
- Takes 1-2 hours (much shorter than LDD)
- Only 2 blood draws for dogs and 3 for cats
- Sensitivity 80-85% for PDH in dogs
- Creates baseline for therapeutic monitoring

ACTH Stimulation Test

Advantages
- Fewer false positives due to stress than LDD
  - Only 14% of dogs with non-adrenal disease have elevated ACTH stim
- Best test for identifying iatrogenic HAC
- Can also test for hypoadrenocorticism
- Can be used to monitor therapy
- Less affected by glucocorticoid therapy than LDD

ACTH Stimulation Test

Disadvantages
- Cortrosyn much more expensive than dexamethasone
- (ACTH gel hard to find, and must be compounded)
- 15-20% False negatives in dogs with HAC
- Sensitivity only 50% for ADH in dogs
- Sensitivity only 50% for all HAC in cats
- Can not distinguish between PDH and ADH

ACTH Stimulation Test

Dog Protocol 1 – Low Dose Cortrosyn
- 12 hour fast baseline sample
- Administer 1-5 mcg/kg Cortrosyn IV
- 1 hour Post-Cortrosyn sample
- Split leftover reconstituted Cortrosyn into plastic syringes and freeze
- No loss of activity for at least 6 months in the freezer, or 4 months in the refrigerator
**ACTH Stimulation Test**

**Dog Protocol 2 – High Dose Cortrosyn**
- 12 hour fast baseline sample
- Administer 1 vial (250 mcg) Cortrosyn IV or IM (I prefer IV)
- 1 hour Post-Cortrosyn sample
- Possible increased risk (still very low risk) for adrenal necrosis if dog is taking Trilostane

**Dog Protocol 3 – ACTH gel**
- 12 hour fast baseline sample
- Administer 1 mg/lb ACTH gel IM
- Max out at 50 units per dog
- 2 hour Post-ACTH sample

**Cat Protocol 1 - Cortrosyn**
- 12 hour fast baseline sample
- Administer 5 mcg/kg Cortrosyn IV or IM
  - IV is recommended, because ACTH levels are significantly higher, but all cats may not tolerate it
- If given IM:
  - 30 minute Post-Cortrosyn sample
  - 1 hour Post-Cortrosyn sample
- I given IV – one sample at 60-90 minutes

**Cat Protocol 2 – ACTH gel**
- 12 hour fast baseline sample
- Administer 1 mg/lb ACTH gel IM
- 1 hour Post-ACTH sample
- 2 hour Post-ACTH sample
  
  Challenge with giving any ACTH IM is that if given intrafat, no stimulation takes place

**Results**

- **Hypoadrenocorticism**
  - Pre – less than 6
  - Post - less than 6, and less than 2-3x pre
  - Pre and post are often <2
- **Normal**
  - Pre – 0.1-6
  - Post - <20 and >3x pre

- **Iatrogenic Cushing’s**
  - Pre – 5-10
  - Post – 5-10 and less than 2x pre
- **Borderline – stress or sick**
  - Pre – 0.1-6 or more
  - Post – 20-30
- **Hyperadrenal or Severe stress**
  - Pre – 0.1-6 or more
  - Post - >30 or more
**ACTH Stimulation Test**

**Test**
- **Case:** 3 year old SF Land Shark with PU-PD, SAP 315 and normal derm  
  - Pre 12, Post 29  
  - **Suspect stress** – look elsewhere first, come back to LDD if the dog still looks Cushingoid
- **Case:** 4 year old Yorkie with PU-PD and chronic relapsing GI upset  
  - Pre 0.5, post – 1  
  - **Hypoadrenocorticism**

**ACTH Stimulation Test**

**Test**
- **Case:** 11 year old Boston Terrier with PU-PD, endocrine alopecia, SAP 1900, ALT 200  
  - Pre 6, Post 6  
  - **Suspect iatrogenic Cushing’s** – check the medical record for glucocorticoids  
  - **Intratrat injection** – check route of administration
- **Case:** 9 year old Cairn terrier with PU-PD, endocrine alopecia, and who is fat and blue  
  - Pre 12, Post 55  
  - **Probably Hyperadrenocorticism** – confirm with ultrasound

**ACTH Stimulation Test**

**Test**
- **Case:** 11 year old Persian with poorly regulated diabetes mellitus  
  - Pre 8, 30 minute 42, 1 hour 19  
  - **Hyperadrenocorticism** - likely
- **Case:** 9 year old Labrador retriever with PU-PD and hepatomegaly  
  - Pre 1, Post 6  
  - **Probably Normal** – pursue other diagnoses first

**ACTH Stimulation Test**

**Test**
- **Case:** 16 year old MN unregulated diabetic cat whose skin fell off when someone scruffed him  
  - Pre 10, 30 minute 12, 60 minute 19  
  - **Don’t Give Up Yet** – ACTH Stim 50% false negatives in cats, do LDD and ultrasound
- **Case:** 13 year old Schnauzer who presented for sudden blindness, red eyes and PU-PD  
  - Pre 3, Post 66  
  - **Possible SARDs** – recheck 60 days

**Low Dose Dexamethasone Test**

Tests the integrity of negative feedback

**Advantages**
- Takes a full 8 hours – have to plan ahead  
- Dexamethasone much cheaper than Cortrosyn or ACTH gel  
- More sensitive than ACTH stim – will identify 95-98% of dogs with HAC
- Can sometimes distinguish between PDH and ADH

**Disadvantages**
- 3 blood draws for dogs and 5 for cats  
- More false positives due to stress  
  - 40-50% of dogs with non-adrenal disease had inadequate suppression at 4 and 6 hours
- No baseline for therapeutic monitoring  
- Not a good test for identifying iatrogenic HAC and cannot detect hypoadrenocorticism  
- Phenobarbital will cause false positive
Low Dose Dexamethasone Test

Protocol - Dog
- 12 hour fast baseline sample 8-9am
- Administer 0.01-0.015 mg/kg dexSP IV
- Diluting dexSP with saline may make dosing more accurate for small patients
- 4 hour post-dex sample
- 8 hour post-dex sample

Protocol - Cat
- It can be helpful to place jugular catheter the day before if cat resents venipuncture
- 12 hour fast baseline sample 8-9am
- Administer 0.1 mg/kg dexSP IV
- 2 hour post-dex sample
- 4 hour post-dex sample
- 6 hour post-dex sample
- 8 hour post-dex sample

Low Dose Dexamethasone Test

Results - Dogs
- Suppression – cortisol falls below 1.5, or 50% of baseline
- Suppression at 4 and 8 hours is normal
- May not suppress fully until 8 hours if stressed
- Suppression at 4 hours, and then “escape” back to baseline at 8 hours suggests PDH or stress
- Lack of suppression at all means either advanced PDH or ADH – confirms HAC
  - Do an ultrasound

Test
- Case: 14 year old SF Dachshund with polycythemia, lung disease and endocrine alopecia
  - Pre 7, 4 hour 1.2, 8 hour 10
  - PDH
- Case: 10 year old SF biting Cocker Spaniel with bilateral ruptured cruciates, SAP 2500, ALT 400
  - Pre 12, 4 hour 10, 8 hour 1.0
  - Normal – look for other causes

Low Dose Dexamethasone Test

Test
- Case: 7 year old Sheltie with hyperlipidemia, SAP 2500, ALT 1890, and skin disease
  - Pre 7, 4 hour 0.4, 8 hour 1.3
  - Normal – look elsewhere for cause, do ACTH stim or repeat LDD or ACTH stim in 6 months
- Case: 10 year old MN Blue Heeler with PU-PD, endocrine alopecia and highly regenerative anemia
  - Pre 12, 4 hour 10, 8 hour 10
  - HAC – PDH or ADH, do differentiating test (US Abdomen first)

Abdominal Ultrasound
Abdominal Ultrasound

- Large, hyperechoic liver (relative to fat)
- Two plump adrenals indicates PDH or chronic stress
  - 7.5 mm is upper limit of adrenal thickness in the dog
- ADH – one large and one small adrenal
  - Benign ADH often 10-20mm
  - Most adrenals > 20 mm are ADH (often malignant)
  - Nearly all adrenals > 40 mm are malignant

Ancillary Diagnostics

- Liver cytology – steroid hepatopathy
- Adrenal cytology not usually helpful
- Can give a great deal of information about a systemically ill patient, in case HAC is not the primary problem
High Dose Dexamethasone Test

Advantages
• Distinguishes between PDH and ADH 70-75% of the time
  – 25% of PDH do not suppress
• Can therefore characterize multiple adrenal nodules
• Much easier sample handling than Endogenous ACTH

Disadvantages
• Doesn’t always distinguish between ADH and severe PDH
• Takes all day – have to plan ahead
• Have to take 5 samples from a cat

Protocol - Dog
• 12 hour fast baseline sample 8-9am
• Administer 0.1 mg/kg dexSP IV
• 4 hour post-dex sample
• 8 hour post-dex sample

Protocol - Cat
• It can be helpful to place jugular catheter the day before
• 12 hour fast baseline sample 8-9am
• Administer 1 mg/kg dexSP IV
• 2 hour post-dex sample
• 4 hour post-dex sample
• 6 hour post-dex sample
• 8 hour post-dex sample

Results
• Suppression on HDD but not LDD confirms PDH in dogs and cats
• Lack of suppression on both LDD and HDD suggests ADH, but can also be severe PDH in dogs
  – not particularly helpful
• Rarely done in practices with US

Endogenous ACTH
PDH – High ACTH - >40-45 pg/ml
ADH - Low (undetectable) - <20 pg/ml
• Diagnostic 75% of the time in dogs
• 4% of results are incorrect in dogs
• Technically difficult and expensive to ship
  – Spin and separate plasma immediately
  – Add protease inhibitor apritinin
  – Freeze and ship THAT DAY overnight frozen
  – Dry ice especially important if no apritinin
  – In plastic tube
  – To Michigan State (consult lab before sending)
Atypical ACTH Stim

- When your gut tells you the patient is Cushingoid, but your tests dash your hopes
- Same protocol for ACTH stim
- Tests for:
  - Cortisol, Aldosterone
  - Estradiol, Androstenedione
  - 7-Hydroxyprogesterone, Progesterone
- Send to Tennessee

Atypical Hyperadrenocorticism

- A subset of adrenal HAC (UTen Handout)
  - ultrasound can help identify candidates
  - As can Low DoseDex (*no* 4 hr suppression)
- Adrenal tumor or congenital hyperplasia
- Symptoms are similar
  - PU-PD
  - Temperament changes
  - Thin skin, endocrine alopecia
  - Elevated bile acids
  - Concurrent diabetes mellitus not uncommon

Baseline Cortisol

**Screening for hypoadrenocorticism**
- >2 µg/dL – hypoadrenocorticism highly unlikely if not receiving prednisone
- <2 µg/dL - little information obtained

**Monitoring hyperadrenocorticism**
- >1.3 µg/dL - excludes excessive suppression in dogs undergoing trilostane therapy
- <2.9 µg/dL - excludes inadequate control in dogs undergoing trilostane therapy
- 1.3-2.9 µg/dL or 50% of the pretreatment baseline cortisol - acceptable control in dogs undergoing trilostane therapy

Treatment

- Trilostane
- Mitotane, Lysodren, o,p-DDD
- Ketoconazole
- Surgery
  - Hypophysectomy
  - Adrenalectomy
- Radiation Therapy
- Selegeline, L-Deprenyl
- Other
  - Metrapone
  - Mifepristone

Trilostane

**How Does It Work?**
- Blocks the enzyme in the adrenal gland that makes both cortisol and aldosterone
- Competes for 3-beta-hydroxysteroid dehydrogenase
- May not ameliorate signs of high androgens, if present
- Also decreases aldosterone, progesterone and androstenedione
- No separate induction and maintenance periods

**How Does It Work?**
- Give with food to maximize absorption
- Takes effect within 24 hours
- PU-PD, polyphagia improve within a week
- Coat regrowth, increased energy, weight loss, take 6 months or more
- Pseudomyotonia may never completely resolve
  - Some have tried procainamide
- Sudden deaths due to acute adrenal necrosis are rare, but do happen
**Trilostane**

*When is it Used?*
- First line therapy for dogs with ADH and PDH
- Holds promise for cats with PDH
  - One study so far (Mellet Keith et al, 2013)

*Trilostane*  
**Dose** – 10mg, 30mg, 60 mg & 120 mg caps **5 mg coming soon**
- Start at 2 mg/kg PO per day (divide BID if possible)
  - lower than the package insert
  - BID works better for diabetics
- Dispense prednisone to keep on hand
  - 0.05-0.1 mg/lb/day
- Stop meds and come in ASAP if vomiting, diarrhea, not eating, not drinking, weakness, etc.
- Some call frequently to check

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**Trilostane** *(1-3 capsules per day)*

- **Dogs <10kg**
  - 10mg PO SID
- **Dogs 10-15kg**
  - 10mg PO BID
- **Dogs 15-20kg**
  - 30mg PO SID
- **Dogs 20-25kg**
  - 30mg am, 10mg pm
- **Dogs 25-30kg**
  - 30mg am, 20mg pm

- **Dogs 25-30kg**
  - 30mg PO SID
- **Dogs 30-35kg**
  - 30mg PO am, 40mg pm
- **Dogs 35-40kg**
  - 60mg am, 20mg pm
- **Dogs 40-45kg**
  - 60mg am, 30mg pm
- **Dogs 45-50kg**
  - 60mg am, 40mg pm

**Trilostane** *(1-3 capsules per day)*

- **Dogs 25-30kg**
  - 60mg PO SID
- **Dogs 30-35kg**
  - 30mg PO am, 40mg pm
- **Dogs 35-40kg**
  - 60mg am, 30mg pm
- **Dogs 40-45kg**
  - 60mg am, 30mg pm
- **Dogs 45-50kg**
  - 60mg am, 40mg pm

**Monitoring – Baseline Cortisol & Electrolytes**
- Every 3 weeks until optimal regulation
- Then every 3-4 months for the first year
- Then every 6 months
- Test 2-4 hours after Trilostane
- Some prefer ACTH stim & electrolytes
- If you overshoot, reduce dose by 50% until symptoms recur

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**Lysodren**

*How Does It Work??*
- Progressive necrosis of the adrenal glands

*Which Zones Does It Affect??*
- Cortex only (not medulla)
  - Zona glomerulosa
  - Zona fasciculata
  - Zona reticularis

**Induction**
- Bring adrenal gland function to normal or just below normal in 5-14 days
  - ADH – takes longer

**Maintenance**
- PDH - Keep adrenal function just below normal, so adrenal glands can not respond to excessive ACTH
- ADH – Reduce adrenal hypertrophy to normal or just below
  - ADH – takes more Lysodren

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**Lysodren – Two Treatment Phases Goals of Therapy**

**Induction**
- Bring adrenal gland function to normal or just below normal in 5-14 days
  - ADH – takes longer

**Maintenance**
- PDH - Keep adrenal function just below normal, so adrenal glands can not respond to excessive ACTH
- ADH – Reduce adrenal hypertrophy to normal or just below
  - ADH – takes more Lysodren
Lysodren – Induction

Lysodren Dose
• Books say 50 mg/kg/day for 7-10 days
  – This is great for profoundly Cushingoid dogs
  – And for dogs with adrenal tumors
  – Or for dogs who fail induction at a lower dose
• I often start at 25 mg/kg/day for 7-10 days, if:
  – Cushing Syndrome due to PDH is not yet profound
  – Owner is less than totally vigilant
  – Worried about false positive test results

To Reduce Side Effects
• Divide dose BID
• Give with meals

To Give Pred or Not Give Pred
– PRO: patient will feel better
– PRO: patient less likely to crash if owner not paying attention
– CON: more likely to cover up clinical signs of end point, and overshoot
– CON: could theoretically interfere with ACTH stim
– Either way, always dispense pred for owner to have on hand
– DOSE: 0.05-0.1 mg/lb/day

Identifying the End Point
• Clinical Signs for owner to watch for
• Should they occur – stop Lysodren and come in for ACTH stimulation test; give pred if really worried
  – Poor appetite
  – Vomiting, Diarrhea
  – Water consumption drastically decreased
  – Lethargy
• ACTH stim
  – If no end point noted in 7-10 days, do anyway
  – GOAL: Post stimulation cortisol less than 5-10ug/dl
  – Or Post stim <15 and clinical signs controlled

If End Point is not reached after the first round
• If End Point is nowhere in sight
  – 50 mg/kg/day for 5-7 more days
  – May have to dose 75-80 mg/kg/day or more if ADH
• If significant progress has been made
  – Same dose for 5-7 more days

MAKE SURE OWNERS FULLY UNDERSTAND INDUCTION
• Go over medications in the exam room
• Make sure medications are labeled properly
• Provide a handout which explains the process
• Have owners make appointment for recheck before they leave
• Call to check on patient every 3 days, and if they “no show” an appointment
• Make sure there is access to emergency veterinary care that can handle the case

Lysodren – Maintenance

• Daily dose required for induction given once to twice weekly
• If induction is overshot
  – No response at all to ACTH stimulation
  – May not show adverse clinical signs
  – Stop Lysodren and recheck ACTH stim 30 days
  – Give Pred + mineralocorticoids if needed
• If relapse occurs, repeat induction
Lysodren for ADH
• May have to dose 75-80 mg/kg/day or more if ADH
• 50% will take more than 2 weeks to induce
• Some as long as 30-60 days or more
• Use Low Dose Pred during induction
• May also need mineralocorticoids during induction
• Many need pred ± Flurinef in maintenance
• 50% will experience adverse drug reactions

Lysodren – Side Effects
• Anorexia, vomiting, diarrhea (blood)
• Lethargy, weakness, ataxia
• Idiosyncratic hepatotoxicity
• CNS toxicity
• Transient or permanent hypoadrenocorticism
• Bone marrow necrosis

Lysodren – Monitoring
• ACTH stims as needed for induction
• Then twice yearly
• Rechecks when doing well:
  – CBC
  – Liver enzymes
  – Electrolytes
  – ACTH stim
• Recheck every 3-4 months in the first year
• Then every 6 months when stable
• More often if patient not doing well
• Lysodren is preferred for diabetic cushingoids

Medical Adrenalectomy
High Dose Lysodren
• 50-75 mg/kg/day for 25 days
• No maintenance therapy needed
• Pred + mineralocorticoids must be supplemented during induction and life long
• 25% over shot the end point – life threatening
• 86% achieved remission
• 43% relapsed
• 61% alive three years later

Ketoconazole
How Does It Work?
• Inhibits enzyme system involved in both androgen and cortisol production
• CYTP450
• Also inhibits ACTH secretion

Ketoconazole
Protocol
• 5 mg/kg PO BID x 7 days
• Then 10 mg/kg PO BID, if tolerated well
• ACTH stimulation test at 21 days
• ACTH stim several hours after drug administration
• Increase in 5 mg/kg increments until ACTH stim shows good control
• Most dogs require 15 mg/kg PO BID
**Ketoconazole**

**Side Effects**
- Transient signs of low cortisol
- GI upset
- Hepatotoxicity

**Selegiline**

**How does it work?**
- Selegeline is an MAO-B (monoamine oxidase-B) inhibitor
- MAO-B breaks down dopamine
- Dopamine and serotonin apply negative feedback to the pars intermedia, and reduce ACTH
- MAO-B inhibitors will increase dopamine levels
- Thus inhibit ACTH production by the pars intermedia

**Selegiline**

- Selegline works only of the excessive ACTH production is coming from the pars intermedia (PDH)
- 80-85% of dogs with HAC have PDH
- Only 15-25% of dogs with PDH have a pars intermedia tumor
- 12-21% of dogs with HAC may respond to Selegline
- No known antemortem test to distinguish pars intermedia PDH from pars distalis PDH

**Selegiline**

- Pergolide is a similar dopaminergic used similarly in horses
- Bromocriptine is another dopamine agonist, but is not effective for PDH in dogs

**Dose**
- 2 mg/kg PO SID

**Adrenal Surgery**

**Pre-Operative chemotherapy**
- To improve clinical signs and improve general condition of the patient
- In an attempt to decrease risk of surgery
- Thromboembolism in particular
- Trilostane and ketoconazole are probably preferred
- Lysodren may be used to shrink large or invasive tumors

**Adrenal Surgery**

**Procedure**
- Mineralocorticoids and glucocorticoids perioperatively
- Ventral midline or flank approach
- Steroids tapered over 2-3 weeks

**Bilateral adrenalectomy has been performed in PDH dogs who are refractory to medical therapy**
### Radiation Therapy
- Of course, only for PDH
- 3/12 dogs euthanized prior to end of 1 month study
- 6/12 experienced improvement in clinical signs
- 4/12 in remission at the end of the study
- Some do well, but not uniformly effective

### Hypophysectomy
- Of course, only for PDH
- Guided by MRI or CT
- Sphenoid bone ventral to pituitary removed
- Transoral or ventral cervical approach
- 50% of dogs with PDH have tumors less than 3 mm in diameter
- The entire pituitary is removed

### Hypophysectomy
- Surgically induced hypothyroidism and hypoadrenocorticism are expected
- Lifelong thyroid and corticosteroid supplementation are required
- If the hypothalamus is damaged, central diabetes insipidus may result
- Desmospressin (DDAVP) is usually administered for 2 weeks post-op and may need to be supplemented lifelong

### Ancillary Treatments
- Hypertension often resolves when HAC goes into remission
- Hyperlipidemia often resolves when HAC goes into remission
- Antibiotics for UTI
- Radiation for macroadenomas
  - Ameliorates neuro signs, but not HAC

### Prognosis
#### Lysodren Therapy
- 80-90% will achieve remission
- 50% will have relapse and need to be induced again
- 25% PDH will have adverse drug reactions during induction
- Median survival 2-2.5 years
- Unknown prognosis for ADH

#### Trilostane Therapy
- 60-70% will achieve remission
- Less than 15% of dogs experience signs of low cortisol
- Side effects can quickly be dealt with by decreasing dose
- Median survival 2-2.5 years
**Ketoconazole Therapy**
- 75% respond
- Works equally well with PDH and ADH
- 25% do not respond – perhaps due to variable GI absorption
- If given for years, liver toxicity may develop
- Median survival unknown

**Hypophysectomy**
- 7% die within 4 weeks of surgery
- 85% have complete remission
- 21% relapse
- 6% have persistent disease
- 30% develop KCS
- Median survival 2 to 2.5 years

**Radiation Therapy**
- 25% euthanized within 1 year
- 33% have complete remission
- Unknown number relapse
- 50% have persistent disease
- Median survival unknown

**Adrenal Surgery**
- 20-30% will not survive surgery (2 weeks)
- Distinguishing benign from malignant on histopath is challenging (50/50)
- Evidence on metastasis on surgery is the most telling
- Those with benign ADH who survive surgery are likely to be cured
- Those with malignant ADH who survive surgery will likely die of their disease in 2-2.5 years

**Bottom line**
- Most dogs will survive 2-2.5 years if treated
- Most euthanized within 1-2 years if not treated
- Quality of life if treated is usually significantly better if treatment is well tolerated
- Some dogs respond very well, have few side effects, and live longer than 3 years
- Some dogs have unacceptable side effects, including death
- Some dogs bloodwork says they are well controlled, but symptoms are not

**Feline Hyperadrenocorticim**
- 80% of cats with hyperadrenocorticim are diabetics
- Progesterone secreting tumors cause the same clinical signs as cortisol secreting tumors
- Clinical Signs (other than dysregulated DM):
  - Pot belled appearance
  - Thin, seborrheic slow growing haircoat
  - Muscle weakness
  - Skin fragility
  - CNS signs if macroadenoma

**Prognosis**
Summary

- **PowerPoint Handout** goes behind the yellow tab

- **Laboratory Information**
  - MSU Endocrine Lab Form
  - MSU Lab Fee Schedule
  - MSU Reference Ranges
  - UTenn Endocrine Lab Form
  - UTenn Submission Guidelines
  - UTenn HAC Treatment Guidelines

Summary

- **Vet Handouts**
  - Summary of Adrenal Testing
  - UTenn Atypical ACTH Stim Testing
  - UTenn Treatment Considerations for HAC
  - Diagnosis and Treatment of Hyperlipidemia

- **Client Handouts**
  - Canine Hyperadrenocorticism
  - Classifying Hyperadrenocorticism
  - Treating Adrenal Hyperadrenocorticism
  - Treating Pituitary Hyperadrenocorticism
  - Treating Hyperlipidemia

Summary

- **Drug Information Handouts**
  - Ketoconazole
  - Mitotane
  - Selegiline
  - Triostane

Acknowledgements


