

## 1 **Update: Hyperadrenocorticism in Dogs**

Lauren Prause, DVM, MS DACVIM (Internal Medicine)

Jennifer Lowry, DVM, MS, DACVR

Peak Veterinary Specialists

## 2 **Hyperadrenocorticism**

### ❖ Canine Cushing's Syndrome (CCS)

#### ➢ Pituitary-dependent=Cushing's disease

\* macroadenoma

#### ➢ Adrenal dependent

\* Adrenocortical carcinoma

\* Adrenocortical adenoma

#### ➢ Iatrogenic

### ❖ Atypical HAC

## 3 **"Atypical" Cushing's**

### ❖ Secrete excess cortisol in almost every case

### ❖ May have a "blockade" in cortisol synthesis causing an increase in cortisol precursors

### ❖ Result- looks cushingoid, ACTH stim=normal

### ❖ Adrenocortical tumors

#### ➢ Cortisol secreting

#### ➢ Aldosterone

#### ➢ "incidentaloma"

## 4 **"Atypical" Cushing's**

### ❖ Variances in clinical signs may be due to other hormone secretion:

#### ➢ Aldosterone

#### ➢ Progesterone, 17Alpha-OH-progesterone

#### ➢ Estrogens

#### ➢ Androgens

#### ➢ 11-deoxycortisol, deoxycorticosterone

## 5 **Clinical Features**

### ❖ Signalment-

#### ➢ F>M

#### ➢ Median age=10y

### ❖ Clinical signs

#### ➢ Most common: polyuria/polydipsia, polyphagia, panting, abdominal enlargement, endocrine alopecia

## 6 **Clinical Features**

### ❖ Pituitary macroadenoma syndrome

\* Neuro signs usually develop 6mo post dx

\* 10-20% have neuro signs at the time of diagnosis

\* Dull, listless, stupor- most common

\* Inappetance

\* Aimless wandering, pacing, ataxia

- \* Head pressing, circling
- \* Behavioral alterations
- \* Autonomic signs- adipsia, loss of temperature regulation, erratic heart rate, inability to be roused from sleep-like state

## 7 **Initial Work-Up**

**1**

- ❖ CBC
- ❖ SADP
- ❖ UA, culture
  - +/- U P:C ratio
- ❖ BP

**2**

- ❖ Neutrophilic leukocytosis
- ❖ Eosinopenia
- ❖ Lymphopenia
- ❖ Mild erythrocytosis
- ❖ Incr. ALP, AST
- ❖ Increased cholesterol, lipemia
- ❖ Hyperglycemia
- ❖ Hyposthenuria, isosthenuria,
- ❖ UTI, proteinuria
- ❖ Hypertension

## 8 **Medical complications**

- ❖ Pituitary Macroadenoma syndrome
- ❖ PTE
- ❖ Systemic hypertension
- ❖ Cystic calculi, GN, proteinuria
- ❖ CHF
- ❖ Pancreatitis
- ❖ DM

## 9 **Further Diagnostics**

- ❖ ACTH stimulation test
- ❖ LDDS
- ❖ HDDS
- ❖ Abdominal ultrasound
- ❖ Endogenous ACTH
- ❖ Urine cortisol creatinine
- ❖ CT/MRI

## 10 **Treatment**

- ❖ Background
- ❖ Medical Management
  - Tried and True
  - New
- ❖ Radiation Therapy
- ❖ Surgery
  - Hypophysectomy
  - Adrenalectomy

11  **Tried and true treatment**

- ❖ o,p'-DDD (Lysodren, Mitotane)
  - Destruction of the adrenal cortex
  - Selective protocol
    - \* 50mg/kg divided BID for 5-10 days
    - \* Maintenance - 50mg/kg q7-10d
      - Divided in 2-3 doses
      - (26-330 mg/kg/wk)
    - \* ACTH stim - 2-6ug/dl (1-5ug/dl)
  - Non-selective protocol (Utrecht protocol)

12  **Lysodren**

- ❖ Side effects (20-25%)
  - Gastric irritation
  - Addisonian crisis, iatrogenic hypoadrenocorticism
  - Neurologic signs
- ❖ Relapse- nearly 50% within first year
  - Usually increase dose by 50% after reinduction

13  **Trilostane (Vetoryl®)**

- ❖ In use in Europe since 1997
- ❖ Approved for use in US-2008
- ❖ Competitively inhibits steroid synthesis
- ❖ Dose variability
- ❖ Monitor with ACTH stim test
  - 40-150 nmol/L
  - 2-5ug/dl

14  **Trilostane**

- ❖ Starting dose- variable!
  - 2-5mg/kg daily-manufacturer recommends
  - 2.5mg/kg daily, up to 15 (Daminet, 2006)
  - 6mg/kg daily, mean final 4-15 (Scott-Moncrieff, 2006)
  - Per dog weight:
    - \* 5-20kg=60mg q 24h
    - \* 21-40kgs=120mg q 24h
    - \* >40kgs=120-240mg q 24h

15  **Trilostane**

- ❖ Maintenance
  - Increase in 10-30mg increments
  - May be dosed BID
  - Will need dose adjustments (50%)

16  **Trilostane- once or twice?**

- ❖ Twice daily dosing -Vaughan, et al (2008)

- 22 dogs
- Lower dose, 0.5-2.5mg/kg BID
- mean 1.9mg/kg- good response
- Mean serum post ACTH stim
  - \* 3-4 after admin=2.6ug/dl
  - \* 8-9 after admin=8.09ug/dl
- Results: potent and effective, low dose BID

17  **Trilostane- once or twice?**

- ❖Feldman et al (2007)
  - Large percentage of dogs escaped control with once daily dosing
- ❖Arenas et al (2006)
  - Consistent efficacy with BID dosing

18  **Trilostane-Once or twice?**

- ❖11 dogs- once daily (Ruckstuhl et al, '02)
  - PU/PD- decr. in 7 weeks, 50% resolution-12 weeks
  - Derm- resolved in all dogs by 12 months
- ❖78 dogs- once daily (Neiger et al, 2002)
  - PU/PD- resolved 70% in 4 weeks
  - Derm- resolved 62% in 4 weeks
- ❖44 dogs- BID dose (Alenza et al, 2006 )
  - PU/PD- resolved 100% after 4 weeks
  - Derm- resolved within 6 months

19  **Trilostane**

- ❖Monitor with ACTH stim test
  - 4-6 hours post administration
  - 10, 30, and 90 days
  - 30 days after each dose adjustment
- ❖Goal- 1-5ug/dl
  - <1ug/dl- discontinue for 48-72 hours, restart at lower dose

20  **Trilostane**

- ❖Dosage
- ❖Side effects
  - Vomiting, diarrhea, lethargy
    - \* Mild, self-limiting- 63%
  - Neutropenia?
  - Hypoadrenocorticism

21  **Trilostane vs. Lysodren**

- ❖Effectiveness
- ❖Side-effects
- ❖Survival
- ❖Cost

22  **Survival**

- ❖ Baker et al- (2005)
  - Not significantly different,
  - Median= 662 and 708 days
- ❖ Arenas et al- (2006)
  - 3 year study
  - Median for lysodren – 24 months
  - Median for trilostane BID – 30 months

23  **Other treatments-Ketoconazole**

- ❖ Ketoconazole (Nizoral)
  - 30mg/kg divided q 12 hours
  - Side effects: vomiting, anorexia
  - Disadvantages- cost, daily medication, poor control
  - Use- pre-surgical stabilization of adrenal tumors

24  **Other treatments- Anipryl**

- ❖ L-deprenyl (Anipryl)
  - *“Because of their limited efficacy and/or potential side effects, ketoconazole and L-deprenyl will not be discussed”*
  - Increases CNS dopamine to decrease cortisol
  - Effective <20%
  - Side effects uncommon
  - Disadvantage- cost, daily medication, effectiveness

25  **Other treatments**

- ❖ Unilateral adrenalectomy- ADH choice tx
- ❖ Bilateral adrenalectomy
  - PDH with poor response to medical management
  - Disadvantages:
    - \* Risk of surgery in poorly controlled dog with PDH
    - \* Cost
    - \* Permanent hypoadrenocorticism

26  **Ultrasound**

- ❖ Presented by Dr. Jennifer Lowry