

Treatment Option Considerations
Steroid Profiles in the Diagnosis of Atypical Cushing's Disease
Clinical Endocrinology Service/College of Veterinary Medicine/University of Tennessee

Where positive test results of increased adrenal activity are present, consider the need for:

- 1) **Ultrasound and/or Endogenous ACTH.** Procedures to rule out primary adrenal tumor presence.
- 2) **Melatonin.** Often used as a first treatment, especially if alopecia is present, since it is cheap, has few side effects and is available in health food stores or via nutrient suppliers on the Internet. Typically, a dose of 3 mg is given q12hrs (BID) for dogs <30 lbs; a dose of 6 mg is given q12hrs (BID) for dogs > 30 lbs. Regular melatonin is usually used rather than rapid release or extended release products. Melatonin has anti-gonadotropic activity (effective for ferret adrenal disease), and it inhibits aromatase enzyme in tissues (decreases androstenedione and testosterone conversion into estradiol) and 21-hydroxylase enzyme (effectively lowers cortisol level). Allow at least 4 months for treatment effects to be effective. Response time is variable between dogs. Monitor treatment effectiveness by improvement in clinical signs, biochemistries or by repeat of steroid profile.
- 3) **Melatonin Implants.** Available for dogs and ferrets. (WWW.MELATEK.NET). Sizes are 8, 12 and 18 mg for <25, 25-50 and >50 lb dogs, respectively. Effects last 3-4 months.
NOTE: *Melatonin and flax hull product with lignans are used together when estradiol is increased.*
- 4) **Lignan.** Lignan has phytoestrogenic activity, and competes with estradiol for tissue estrogen receptors, with less biological effect. Lignan also inhibits aromatase enzyme (lowers estradiol) and 3-beta HSD enzyme (lowers cortisol). Use either FLAX HULL (SDG) lignan, or HMR lignan. See LIGNAN at our website under TREATMENT for details. **DO NOT USE** flax seed oil as the lignan content is very low, and the flax oil can increase triglycerides. **SOURCES OF APPROPRIATE PRODUCTS are listed at the website.** Lignans are safe, so doses don't have to be exact. Suggested doses: SDG lignan; one milligram/lb B. Wt./day. HMR lignan; 10-40 mg/day for small to large dogs.
- 5) **Maintenance dose of Lysodren™.** Often useful in combination with melatonin and lignan to help lower sex steroid levels other than estradiol, along with suppressive effect on cortisol level. **NOTE:** **MONITOR CORTISOL LEVELS AS FOR TYPICAL CUSHING'S TREATMENT.**
- 6) **Lysodren™, traditional treatment for Cushing's disease.** Very effective in lowering cortisol, progesterone, androstenedione and 17-hydroxyprogesterone levels. **NOTE:** *Estradiol is not always suppressed by Lysodren™. A baseline estradiol level 1 month post-Lysodren will determine efficacy.*
- 7) **Trilostane.** Now available in the U.S. as Vetoryl™ from Dechra Veterinary Products. **NOTE:** *Trilostane always increases 17-hydroxyprogesterone (some cross-reactivity with pregnenolones in assays??), and frequently increases estradiol and androstenedione as well. Lysodren™ may be preferred for Atypical Cushing's cases.* **FURTHER NOTE:** *Care should be used in switching from trilostane to Lysodren™. Allow adequate time for either drug's effects on the adrenals to subside before switching treatments. (E.g., one month off drug; normal or increased stim-cortisol levels).*
- 8) **Ketoconazole. Cushing's disease treatment.** Effective for increased cortisol and sex steroid levels. Consider 6 to 12 mg/kg, BID along with melatonin and lignan as above. See write-up at our website (and the recent article on ketoconazole treatment at JAVMA, 233:1896, 2008).
- 9) **Selegiline (Anipryl™).** A less used alternative Cushing's disease treatment. See Plumb's Formulary.
- 10) **Hormone cream exposure.** Products may contain estrogen/progestins/testosterone; may result in high serum levels of estradiol and progestins, as well as nipple, vulva, and clitoris enlargement.
- 11) **Ovarian remnant detection.** hCG stim test (estrus) and measurement of progesterone is indicated.
- 12) **Retained testicle detection.** hCG stim test and measurement of testosterone is indicated.
- 13) **For further information** on our Service (e.g., submission, shipping, protocols, treatment, review articles) see our website (www.vet.utk.edu/diagnostic/endocrinology). *Revised 07-19-11.*