

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 (*decreases androstenedione and testosterone conversion into estradiol*) and 21-hydroxylase enzyme (*effectively lowers cortisol level*). 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 lignan from FLAX SEED HULLS (or HMR lignan). **DO NOT USE** flax seed oil as the lignan content is very low, and the flax oil can exacerbate pancreatitis in dogs (triglyceride levels may increase). Search for **standardized products** (via Google or health food stores) that allow determination of lignan content. Available products allow for flexible dosing, and the suggested approximate daily dose of lignan is one milligram (mg) per pound of body weight.
- 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.** **Alternative Cushing's disease treatment.** Effective for increased cortisol and sex steroid levels. Combine with lignan. See write-up at our website (and JAVMA, 233:1896, 2008).
- 9) **Selegiline (Anipryl™).** **Alternative Cushing's disease treatment.** Increases dopamine in the CNS, with less ACTH release. Different mechanism may allow combination treatments with experience.
- 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 clarification regarding test results,** Contact Dr. Jack Oliver (865-974-5729; joliver@utk.edu). Also, Dr's. Kellie Fecteau or Hugo Eiler are available in Dr. Oliver's absence. (865-974-5638). **Note: Several patterns of hormone increase occur, so doing the complete adrenal panel is advised.**
- 14) **For further information on treatments, drug sources, hyperrestrinism and review articles,** refer to our website (www.vet.utk.edu/diagnostic/endocrinology). The site also includes shipping information, a down-loadable submission form and test protocols. *Revised 10-02-09 (JWO).*

