Cushing's Syndrome (HyperAdrenoCorticism = HAC)

Cushing's Syndrome is a collection of symptoms that stems from the overproduction (spontaneous) or overuse (iatrogenic) of steroids. In general, the goal of Cushing's treatment is to limit the effects of symptoms on quality of life by controlling the amount of steroid circulating.

The body produces steroids as a response to stress via the hypothalamic-pituitary-adrenal (HPA) axis. The pituitary gland at the base of the brain produces ACTH, which tells the adrenal gland to produce cortisol. Cortisol helps control blood sugar, balance weight, and fight infections. Atypical Cushing's may include other adrenal hormones, especially the sex hormones (testosterone, estrogen, progesterone, etc).

Approximately 80% of dogs develop pituitary-dependent (PD) Cushing's, which is due to a small hormone-producing tumor in the brain. 15% are adrenal-dependent (AD), due to a hormone-producing tumor in the adrenal glands, located in the abdomen near the kidneys. The remaining are atypical, coming from other sources, including overuse of steroids to control autoimmune diseases and allergies.

Symptoms:

- Excessive thirst and urination
- Increased hunger
- Panting
- Pot-bellied appearance, muscle wasting
- Enlarged liver
- Truncal alopecia - hair loss usually sparing the head and legs. Rarely itchy
- Thinning skin, easier bruising - due to fragility
- Chronic infections - especially skin. May not be itchy due to steroid effects
- Concurrent diabetes mellitus (or secondary) -- diabetic Cushingoid patients are much harder to control, requiring higher doses of insulin due to insulin-resistance. **Note**: I personally address Diabetes first and start on melatonin, then start lignans 2 weeks later. Some internists recommend treating Cushing's and Diabetes at the same time for best control.

Diagnosis:

Bloodwork may reveal an increased ALKP (alkaline phosphatase) due to the steroid isotype. Often, ALKP is significantly increased while GGT (also cholestasis) and ALT (liver damage) are near normal. Urinalysis often reveals a dilute urine sample with no to little glucose (as compared to diabetes).

Definitive tests:

- ACTH Stimulation test: an injection of ACTH measures the adrenal glands response by testing for overproduction of cortisol. ACTH is a more expensive drug, but the test only takes 2 hours to complete.
- Low-dose Dexamethasone Suppression test (LDDST) - 0.01mg/kg Dexamethasone: may differentiate between PD and AD Cushing's. Relatively inexpensive but requires samples before steroid administration, 4 and 8 hours after IV dexamethasone dose -- an all-day test.
- Abdominal ultrasound: PD Cushing's generally causes bilateral enlargement of the adrenal glands, while AD Cushing's causes one to get bigger while the other gets smaller (due to hormonal feedback loop). The liver often shows "vacuolar hepatopathy" due to steroid and fatty infiltration. Ultrasound helps with staging for the potential of surgery in cases of adrenal-dependent Cushing's.

Treatment:

- Melatonin (3-6mg twice daily) and flaxseed lignans (SDG: 1mg/lb/day; HMR: 10-40mg/day) - bind various enzyme receptors. Most benign treatment option for suspect, mild and atypical Cushing's.
- Vetoryl (trilostane) - reversibly suppresses the adrenal glands. Requires established diagnosis. Can be monitored via ACTH Stim test or 4-hr post-dose baseline cortisol.
- Lysodren (mitotane) - irreversibly kills the adrenal glands. Most side effects. Can only be monitored using the more expensive ACTH Stimulation test. May cause Addisonian crisis (hypoadrenocorticism), an emergency scenario of vomiting, diarrhea, and severe electrolyte imbalances (Na:K ratio < 25).
- If iatrogenic Cushing's, re-evaluate ALL steroid-containing products! Balance treatment of steroid-responsive conditions with quality of life and symptoms (which is why our goal with steroids is lowest effective dose).