



**ANTECH**  
D I A G N O S T I C S

# News

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## HYPERADRENOCORTICISM UPDATE

### NEW THERAPY OPTION (*Trilostane*)

Trilostane (Vetoryl®) is an oral enzyme inhibiting drug that blocks the production of several adrenal steroids, including cortisol and aldosterone. In a recent study, 78 dogs with pituitary-dependent hyperadrenocorticism (PDH) were treated with trilostane for up to 3 years. The dose of trilostane was: Dogs < 5 kg, 30 mg q 24h; 5-20 kg, 60 mg q 24h; > 20 kg, 120 mg q 24h. The study's salient findings included:

- LDDS had a sensitivity of 82% in diagnosing PDH.
- ACTH stimulation had a sensitivity of 60% in diagnosing PDH.
- Steroids were not given concurrently.
- Dogs were re-evaluated at 10 days; and 4, 12 and 24 weeks after starting therapy. Clinical signs and ACTH stimulation tests taken 2-4 hours post-trilostane administration were monitored, and the trilostane dose adjusted if necessary.
- Response to treatment: 70% had improvement of polydipsia, polyuria and polyphagia within 4 weeks of starting therapy. There was marked improvement in skin disease within 3 months of treatment in 62% of the dogs. Clinical signs of hyperadrenocorticism were poorly controlled in 8 dogs. Pre- and post-ACTH concentrations decreased significantly 1-3 weeks after commencing treatment. By day 28, 81% of dogs had post-ACTH cortisol concentrations < 9 µg/dL. Dosage adjustment over the treatment period was made in 45% of dogs. In 2 dogs, medication was stopped due to development of hypocortisolemia, and neither dog needed to resume treatment during the 1.8

and 2.7 years followup, respectively. These results suggested self-cure of PDH, unless the original diagnosis was incorrect or a pituitary tumor became infarcted.

- Trilostane was well tolerated. After 3 years, 65% of dogs were still alive. Of those that died, median survival time was 18 months. Seventeen were euthanized and 9 died spontaneously. In comparison, the mean survival time for PDH dogs treated with mitotane (Lysodren®) was 26 months.
- Adverse effects included transient biochemical abnormalities in a few dogs, namely, mild hyperkalemia, azotemia, hyperbilirubinemia, and hypercalcemia. Two dogs died shortly after beginning trilostane therapy and 2 dogs developed iatrogenic Addison's disease.

Trilostane is not licensed for use in the U. S., and can be obtained only from England with a prescription and new drug waiver permit from the FDA. This would enable importation of a 90-day supply of the drug (for more information, see [www.arnolds.co.uk](http://www.arnolds.co.uk)). To date, U.S. veterinarians using trilostane are pleased with results and report fewer adverse effects as compared with mitotane. However, the senior U. K. author for the published study still prefers mitotane as she believes it to be more efficacious. Trilostane may be useful for a treatment trial in cases where the diagnosis of Cushing's disease is uncertain. Monitor clinical signs and ACTH stimulation tests at 10 days and then again every 3-6 months.

In a second study, trilostane was given to 11 dogs with PDH at the mean starting dose of 6

# HYPERADRENOCORTICISM UPDATE (CONT'D)

mg/kg. The dogs were monitored clinically and by routine blood and urine tests, ACTH stimulation tests, and adrenal gland ultrasonography at 1, 3-4, 6-7, 12-16, and 24-28 weeks after starting therapy. All dogs became more active and had reduced polyuria, polydipsia, and panting. Nine of 10 dogs had reduced polyphagia, and 9 of 11 had improved skin condition. Post-ACTH concentrations decreased within the first week of treatment. Clinical signs resolved in 9 dogs and improved in the other 2 within 6 months of treatment. The adrenal glands increased in size on ultrasonography. One dog was transiently lethargic and one was anorexic. Hyperkalemia was also seen in some dogs and may reflect reduction in aldosterone synthesis. Thus, trilostane treatment was safe and efficacious, and resulted in less common and less severe adverse effects than those typically seen with mitotane treatment. Further evaluation of the safety of trilostane is needed.

References: Neiger et al., *Vet Rec* 150: 799-804, 2002; Ruckstuhl et al., *Am J Vet Res* 63: 506-512, 2002.

## DIAGNOSING ATYPICAL CUSHING'S SYNDROME (17-Hydroxyprogesterone)

As summarized in Antech News (September 2001), serum 17-hydroxyprogesterone (OHP) concentrations can be helpful in the diagnosis of atypical cases of hyperadrenocorticism (HAC), namely, those with normal ACTH stimulation and LDDS test results. Some dogs with HAC could have deranged steroid production pathways, such that certain steroid precursors may be abnormally increased and responsible for the presenting clinical signs, whereas cortisol concentrations are normal.

A retrospective study evaluated 7 dogs with clinical signs and routine laboratory data suggestive of HAC. Four dogs had normal ACTH stimulation and LDDS tests; 3 were ultimately determined to have PDH and 1 had an adrenal tumor HAC. Three dogs had normal ACTH stimulation tests and low cortisol concentrations throughout their LDDS tests. All 3 dogs had adrenal tumors. While resting, OHP concentrations were inconsistently increased in these dogs, all 7 had exaggerated OHP concentrations in response to ACTH administration.

### Conclusion

Elevated post-ACTH OHP (and possibly other adrenal sex hormones) may be useful in confirming a diagnosis in dogs with atypical HAC. Dogs suspected of having HAC, but with normal or low cortisol concentrations after receiving ACTH or low-dose dexamethasone, and no history of steroid administration, should be evaluated for a sex hormone-producing adrenal tumor with OHP testing and adrenal gland ultrasonography.

### Test Submission

The test requires 50 µl of serum collected 1 hour post-synthetic ACTH or 2 hours post-ACTH gel administration. The test can be added on to a previously submitted post-ACTH serum sample, as it is **not** necessary to measure resting (pre-) OHP concentrations.

References: Ristic et al., *J Vet Int Med* 16: 433-439, 2002; Syme et al., *JAVMA* 219: 1725-1728, 2001; Frank et al., *JAVMA* 218: 214-216, 2001.

## LAB TIPS

### Name Changes

- *Ehrlichia equi*, a causal agent of granulocytic ehrlichiosis, has been renamed *Anaplasma phagocytophila*.
- *Ehrlichia platys* has been renamed *Anaplasma platys*.
- *Hemobartonella felis*, the causative agent of feline infectious anemia (FIA), has recently been reclassified as two separate species of *Mycoplasma*. The large form, *Mycoplasma hemofelis* is more pathogenic than the small form *Mycoplasma hemominutum*. Evaluation of the blood smear is an insensitive method of diagnosing FIA. In contrast, Antech's PCR method will detect both forms of these *Mycoplasma* species and can distinguish between them.

### Bartonella Western Blot Titration Test (Test Code S16890)

To evaluate the effectiveness of Bartonella therapy, especially for healthy cats, titration of the pre-treatment antibody level in comparison to the six-month post-treatment antibody level is recommended. A 2-fold or greater decrease in the Bartonella antibody titer is indicative of successful treatment of infection. It is necessary to wait 6 months from the end of therapy to wait for antibody levels to decline, subsequent to treatment.

When requesting the 6-month recheck on a patient, be sure to write "RECHECK" (Test Code S16890) on the Test Request Form, so that Antech can alert Dr. Hardy's reference lab to compare antibody levels to those of the pre-treatment archived serum.