Diagnosing and Treating Cases of Suspected Canine Hyperadrenocorticism or Addison’s Disease

**IMPORTANT:** Review history of any administration of corticosteroids as these may influence the reported results.

### Diagnose

**ACTH Stimulation Test**

**Diagnostic Protocol for Cases of Suspected Canine Hyperadrenocorticism or Addison’s Disease**

1. History, physical exam, CBC, chemistry panel, electrolytes and urinalysis consistent with Canine Hyperadrenocorticism or Addison’s disease
2. Draw baseline cortisol sample.
3. Perform an ACTH stimulation test with Cortrosyn® 5 µg/kg IV or ACTH gel 2.2 U/kg IM.
4. Draw 1-hour cortisol (Cortrosyn®) or 1 and 2-hour cortisol (ACTH gel).

#### Pre- and Post-ACTH

<table>
<thead>
<tr>
<th>Pre- and Post-ACTH</th>
<th>Post-ACTH</th>
<th>Pre-ACTH</th>
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<tbody>
<tr>
<td>&lt;2 µg/dL</td>
<td>2–6 µg/dL</td>
<td>2–6 µg/dL</td>
<td>6–18 µg/dL</td>
<td>18–22 µg/dL</td>
<td>&gt;22 µg/dL</td>
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- **If both results are <2 µg/dL, results are consistent with hypoadrenocorticism**
- **Inconclusive**
- **Normal**
- **Equivocal, Cushing’s possible**
- **Consistent with Cushing’s**

5. Begin treatment with mineralocorticoid and/or glucocorticoid as appropriate.

6. Perform high-dose dexamethasone* suppression to discriminate between PDH and ATH, ACTH level and/or abdominal ultrasound.

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*Do not exceed 0.1 mg/kg of dexamethasone.
Diagnose

Low-Dose Dexamethasone Suppression Protocol
For Cases of Suspected Canine Hyperadrenocorticism

- History, physical exam, CBC, chemistry panel, electrolytes and urinalysis consistent with Canine Hyperadrenocorticism
  - Draw baseline cortisol sample.
  - Perform a low-dose dexamethasone suppression test with 0.01 mg/kg of dexamethasone IV.
  - Draw 4-hour and 8-hour cortisols; run 8-hour first and 4-hour may not be indicated.

<table>
<thead>
<tr>
<th>4 hours</th>
<th>8 hours</th>
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<tbody>
<tr>
<td>not needed</td>
<td>&lt;1 µg/dL</td>
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<tr>
<td>1–1.5 µg/dL</td>
<td>1–1.5 µg/dL</td>
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<tr>
<td>&gt;1.5 µg/dL and &gt;50% of baseline</td>
<td>&gt;1.5 µg/dL and &gt;50% of baseline</td>
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<td>&lt;1.5 µg/dL or &lt;50% of baseline</td>
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<tr>
<td>Normal</td>
<td>Inconclusive; consider repeating in 8–12 weeks*</td>
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<tr>
<td>Consistent with Cushing’s</td>
<td>Consistent with PDH</td>
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<td>Consistent with PDH</td>
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<tr>
<td>Perform high-dose dexamethasone** suppression, endogenous ACTH concentration and/or abdominal ultrasound to discriminate between PDH and ATH.</td>
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</table>

*Wait a minimum of 48 hours before repeating if a technical error in the protocol occurred.
**Do not exceed 0.1 mg/kg of dexamethasone.
High-Dose Dexamethasone Suppression Protocol
For Determination of Pituitary-Dependent vs. Adrenal Tumor Canine Hyperadrenocorticism

Low-dose dexamethasone suppression or ACTH stimulation results consistent with Canine Hyperadrenocorticism

- Draw baseline cortisol sample.
- Perform a high-dose dexamethasone* suppression test with 0.1 mg/kg of dexamethasone IV.
- Draw 4-hour cortisol.
- Draw 8-hour cortisol.

4 hours

- <1.5 µg/dL or <50% of baseline
- >1.5 µg/dL and >50% of baseline

8 hours

- <1.5 µg/dL or <50% of baseline
- >1.5 µg/dL and >50% of baseline

Consistent with PDH

Further testing required to differentiate PDH from ATH. Consider measuring plasma ACTH levels and/or performing an abdominal ultrasound.

*Do not exceed 0.1 mg/kg of dexamethasone.
Mitotane (Lysodren®) Dosing and Monitoring
Treatment of Pituitary Dependent Canine Hyperadrenocorticism

Start loading dose of mitotane therapy: 40–50 mg/kg per day with food.

Observe for decrease in appetite, water intake <60 cc/kg/day, vomiting, diarrhea or lethargy.

7–10 days into loading dose with no adverse effects or clinical response noted.

Discontinue mitotane.
Check Na/K to rule out iatrogenic Addison’s disease. Supplement with prednisone as needed. Recheck via ACTH stimulation test in 3–4 weeks.

Perform ACTH stimulation test.

<1 µg/dL

1–5 µg/dL

>5 µg/dL

<1 µg/dL

Begin maintenance mitotane dosing: 30–50 mg/kg per week in divided doses. Continue for 1 month unless adverse reactions occur.

1–5 µg/dL

Perform ACTH stimulation test.

>5 µg/dL

Discontinue mitotane.
Check Na/K to rule out iatrogenic Addison’s disease. Supplement with prednisone as needed. Recheck via ACTH stimulation test in 3–4 weeks. Restart maintenance therapy when appropriate, but at a lower dosage.

Increase weekly dose or repeat loading dose for 5–10 days. Monitor with ACTH stimulation tests and observe for adverse reactions, as above, then increase weekly maintenance dose.

Repeat the ACTH stimulation test at 3 months and then every 3–6 months thereafter. Use the above response criteria to ensure appropriate mitotane dosing. Should adverse reactions occur at any time during therapy, discontinue mitotane, evaluate patient, perform electrolytes and ACTH stimulation test and treat accordingly.

*If ACTH stimulation is still >5 µg/dL after initial 5–10 days of additional loading, continue loading dose for an additional 5–10 days, observing for adverse reactions.
Trilostane (Vetoryl®) Dosing and Monitoring*
Treatment of Canine Hyperadrenocorticism

Day 1
Start trilostane treatment. Administer 2 mg/kg in morning or 1 mg/kg twice daily with food. Observe for lethargy, decreased appetite, vomiting or diarrhea. If adverse reactions observed discontinue trilostane and evaluate patient.

Day 10–14
Clinical examination and biochemistry profile, including electrolytes. Perform ACTH stimulation test 4 hours after morning capsule.

Post-ACTH serum cortisol <1.5 µg/dL (<40 nmol/L)
Clinically well
Stop treatment for 7 days. Restart at lower dose. RETURN TO DAY 1

Clinical signs of hypoadrenocorticism
Stop trilostane and evaluate patient. CBC and biochemistry profile, including electrolytes. Emergency medical attention may be needed in some dogs. Treat as needed.

Post-ACTH serum cortisol >1.5 µg/dL (>40 nmol/L) and clinically well
Continue treatment at current dose.

Recheck at one month
Clinical examination and biochemistry profile, including electrolytes. Perform ACTH stimulation test 4 hours post-capsule.

Assess degree of clinical improvement.

*Modified from “Treatment and Monitoring of Hyperadrenocorticism” flowchart published by Dechra Ltd., 2009.

The recommendations contained in this document are intended to provide general guidance only. As with any diagnosis or treatment, you should use clinical discretion with each patient based on a complete evaluation of the patient, including history, physical examination and complete laboratory data profile. With respect to any drug therapy or monitoring program, you should refer to product inserts for a complete description of dosages, indications, interactions and cautions.
Significant improvement

- Post-ACTH serum cortisol >9.0 µg/dL (>250 nmol/L)
  - Increase morning dose.
  - RETURN TO DAY 1

- Post-ACTH serum cortisol 6.0–9.0 µg/dL (165–250 nmol/L)
  - Continue on current dose, but monitor clinical signs carefully for recurrence.
  - Recheck with ACTH stimulation test (4 hours after morning capsule) and biochemistry profile with electrolytes at 3 months and then every 3–6 months thereafter.

- Post-ACTH serum cortisol 1.5–6.0 µg/dL (40–165 nmol/L)
  - Continue treatment at current dose.

- Post-ACTH serum cortisol <1.5 µg/dL (<40 nmol/L) and clinically well
  - Stop treatment for 7 days. Restart at lower dose.
  - RETURN TO DAY 1

Clinical signs not well controlled

- Post-ACTH serum cortisol >6.0 µg/dL (>165 nmol/L)
  - Increase once daily dose.
  - RETURN TO DAY 1

- Post-ACTH serum cortisol <6.0 µg/dL (<165 nmol/L)
  - Rule out concurrent illness.

Note: Should adverse effects occur at any time during therapy, discontinue trilostane and evaluate patient. Perform CBC, biochemistry profile with electrolytes and an ACTH stimulation test and treat accordingly.