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:**
     - **Pre-ACTH:**
       - <2 µg/dL: Inconclusive
       - 2–6 µg/dL: Normal
       - 6–18 µg/dL: Equivocal, Cushing’s possible
     - **Post-ACTH:**
       - 18–22 µg/dL
       - >22 µg/dL: Consistent with Cushing’s

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

   - **Pre-ACTH:**
     - 2–6 µg/dL
     - 6–18 µg/dL

6. **Perform high-dose dexamethasone**

   - **Post-ACTH:**
     - <2 µg/dL: Consistent with hypoadrenocorticism
     - 2–6 µg/dL: Inconclusive
     - 6–18 µg/dL: Normal
     - 18–22 µg/dL: Equivocal, Cushing’s possible
     - >22 µg/dL: Consistent with Cushing’s

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*Remaining Cortrosyn® can be aliquoted into 1-mL syringes containing 0.2 mL Cortrosyn each. Store aliquoted syringes for up to six months, or vial can be refrigerated for up to one month.*

**Take care not to 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.

Perform ACTH stimulation test.

<1 µg/dL

1–5 µg/dL

>5 µg/dL

Continuing mitotane loading dose for 5–10 days.* Recheck in 5–10 days. Observe for adverse reactions, as above.

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

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.

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.

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.
**Low-Dose Dexamethasone Suppression Protocol**

For Cases of Suspected Canine Hyperadrenocorticism

1. **History, physical exam, CBC, chemistry panel, electrolytes and urinalysis consistent with Canine Hyperadrenocorticism**

2. **Draw baseline cortisol sample.**

3. **Perform a low-dose dexamethasone suppression test with 0.01 mg/kg of dexamethasone IV.**

4. **Draw 4-hour and 8-hour cortisols; run 8-hour first and 4-hour may not be indicated.**

   - **4 hours**
     - not needed
     - 1–1.5 µg/dL
     - >1.5 µg/dL and >50% of baseline

   - **8 hours**
     - <1 µg/dL
     - 1–1.5 µg/dL
     - >1.5 µg/dL and >50% of baseline

5. **Consistent with Cushing’s**

6. **Consistent with PDH**

7. **Inconclusive; consider repeating in 8–12 weeks*”

8. **Perform high-dose dexamethasone**

   - “**suppression, endogenous ACTH concentration and/or abdominal ultrasound to discriminate between PDH and ATH.”

9. **Normal**

10. **Consistent with PDH**

11. **Consistent with PDH**

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*Wait a minimum of 48 hours before repeating if a technical error in the protocol occurred.
**Take care not to 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 and > 50% of baseline
< 1.5 µg/dL or < 50% of baseline
< 1.5 µg/dL or < 50% of baseline
< 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.

*Take care not to exceed 0.1 mg/kg of dexamethasone.
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

Post-ACTH serum cortisol >1.5 µg/dL (>40 nmol/L) and clinically well
- Continue treatment at current dose.
- Recheck at one month
  - 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.
  - Clinical signs not well controlled
    - Assess degree of clinical improvement.

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

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.

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.

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