Diagnosing and treating cases of suspected canine Cushing’s syndrome or Addison’s disease

PLEASE NOTE: Administration of exogenous steroids or stress related to concurrent illness may affect the results and interpretation of ACTH stimulation test and dexamethasone suppression test. For patient-specific interpretations provided through IDEXX DecisionIQ ™, please view your results in VetConnect® PLUS.

Diagnose

ACTH stimulation test
Diagnostic protocol for cases of suspected canine hyperadrenocorticism (Cushing’s syndrome) or hypoadrenocorticism (Addison’s disease)

**History, physical exam, CBC, chemistry panel, electrolytes, and urinalysis consistent with Cushing’s syndrome or Addison’s disease.**

<table>
<thead>
<tr>
<th>Pre- and Post-ACTH</th>
<th>Post-ACTH</th>
<th>Pre-ACTH: 2–6 µg/dL</th>
<th>Post-ACTH: 6–18 µg/dL</th>
<th>Post-ACTH: 18–22 µg/dL</th>
<th>Post-ACTH &gt;22 µg/dL</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;2 µg/dL</td>
<td>2–6 µg/dL</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Consistent with Addison’s</td>
<td>Inconclusive</td>
<td>Normal</td>
<td>Equivocal, Cushing’s possible</td>
<td>Consistent with Cushing’s</td>
<td></td>
</tr>
</tbody>
</table>

- Begin treatment with mineralocorticoid and/or glucocorticoid as appropriate.
- Rule out nonadrenal causes for clinical signs. If alternate cause not identified, consider additional testing for Cushing’s syndrome, including a low-dose dexamethasone suppression test and abdominal ultrasound.
- Perform an abdominal ultrasound, high-dose dexamethasone* suppression test, and/or an endogenous ACTH concentration to differentiate pituitary dependent Cushing’s syndrome (PDH) from adrenal tumor Cushing’s syndrome (ATH).

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

Low-dose dexamethasone suppression protocol
For cases of suspected Cushing’s syndrome

History, physical exam, CBC, chemistry panel, electrolytes, and urinalysis consistent with Cushing’s syndrome.

Draw baseline cortisol sample.

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

Draw and run 4-hour cortisol.

Draw and run 8-hour cortisol.

4 hours | 8 hours
--- | ---
<1 µg/dL | <1 µg/dL
1–1.5 µg/dL and <50% of baseline | <1 µg/dL
<1 µg/dL | 1–1.5 µg/dL and <50% of baseline
1–1.5 µg/dL and <50% of baseline | 1–1.5 µg/dL and <50% of baseline

Does not support a diagnosis of Cushing’s

Supports a diagnosis of PDH

Rule out nonadrenal causes for clinical signs.

Supports a diagnosis of Cushing’s and does not differentiate PDH and ATH

Perform either an abdominal ultrasound, high-dose dexamethasone* suppression test, and/or an endogenous ACTH concentration to differentiate PDH from ATH.

4 hours | 8 hours
--- | ---
≥1 µg/dL and ≥50% of baseline | >1.5 µg/dL and ≥50% of baseline
≥1 µg/dL and ≥50% of baseline | >1.5 µg/dL and ≥50% of baseline
1–1.5 µg/dL and ≥50% of baseline | >1.5 µg/dL and ≥50% of baseline
1–1.5 µg/dL and ≥50% of baseline | >1.5 µg/dL and ≥50% of baseline
1–1.5 µg/dL and ≥50% of baseline | >1.5 µg/dL and ≥50% of baseline
1–1.5 µg/dL and ≥50% of baseline | >1.5 µg/dL and ≥50% of baseline
1–1.5 µg/dL and ≥50% of baseline | >1.5 µg/dL and ≥50% of baseline
1–1.5 µg/dL and ≥50% of baseline | >1.5 µg/dL and ≥50% of baseline

Treatment may be considered.

Inconclusive

Rule out nonadrenal causes for clinical signs. If alternate cause not identified, consider additional testing for Cushing’s, including an ACTH stimulation test and abdominal ultrasound.

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

High-dose dexamethasone suppression protocol
For determination of pituitary-dependent versus adrenal tumor Cushing’s syndrome

Clinical signs and a low-dose dexamethasone suppression or ACTH stimulation results consistent with Cushing’s syndrome.

Draw baseline cortisol sample.

Perform a high-dose dexamethasone* suppression test with 0.1 mg/kg of dexamethasone IV.

Draw and run 4-hour cortisol.

Draw and run 8-hour cortisol.

<table>
<thead>
<tr>
<th>4 hours</th>
<th>8 hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any number</td>
<td>≤1.5 µg/dL</td>
</tr>
<tr>
<td>Any number</td>
<td>&gt;1.5 µg/dL and ≤50% of baseline</td>
</tr>
<tr>
<td>≤1.5 µg/dL</td>
<td>&gt;1.5 µg/dL and ≥50% of baseline</td>
</tr>
</tbody>
</table>

Supports a diagnosis of PDH

>1.5 µg/dL and ≥50% of baseline

Treatment may be considered.

Does not differentiate PDH fromATH

Perform an abdominal ultrasound and/or an endogenous ACTH concentration to differentiate PDH from ATH.

*Do not exceed 0.1 mg/kg of dexamethasone.
Mitotane (Lysodren®) dosing and monitoring

Treat

Treatment of pituitary dependent Cushing’s syndrome

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

1–5 µg/dL → Continue current weekly dosage.

>5 µg/dL → 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.

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.

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. 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.
Trilostane (Vetoryl®) dosing and monitoring*

Treatment of Cushing’s syndrome

**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**
History, physical exam, chemistry panel, and electrolytes. Perform ACTH stimulation test 4–6 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 Addison’s**
      - Stop trilostane and confirm whether clinical signs are due to Addison’s with an ACTH stimulation test as well as a CBC, chemistry panel, and electrolytes. Emergency medical attention may be needed in some dogs. Treat as needed.
  - >1.5 µg/dL (>40 nmol/L) and clinically well
    - **Recheck at one month**
      - History, physical exam, chemistry panel, and electrolytes. Perform ACTH stimulation test.
      - Assess degree of clinical improvement.
    - **Continue treatment at current dose.**

*Modified from “Treatment and Monitoring of Hyperadrenocorticism” flowchart published by Dechra Ltd., 2019.

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 exam, 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.
**Clinical signs not well controlled**

**Significant improvement**

**Post-ACTH serum cortisol >6.0 µg/dL (>165 nmol/L)**
- Rule out concurrent illness.
- **Evaluate if twice daily dosing needed.**

**Post-ACTH serum cortisol <6.0 µg/dL (<165 nmol/L)**
- Evaluate if twice daily dosing needed.

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

**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.

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

**Post-ACTH serum cortisol <1.5 µg/dL (<40 nmol/L) and clinically well**
- Rule out concurrent illness.
- **RETURN TO DAY 1**

**Post-ACTH serum cortisol 1.5–6.0 µg/dL (40–165 nmol/L)**
- Continue monitoring with history, physical exam, chemistry panel, electrolytes and ACTH stimulation test every 3 months.

**Post-ACTH serum cortisol >9.0 µg/dL (>250 nmol/L)**
- Contact the manufacturer for advice on dosing.

**Post-ACTH serum cortisol 1.5–6.0 µg/dL (40–165 nmol/L)**
- Continue monitoring with history, physical exam, chemistry panel, electrolytes and ACTH stimulation test every 3 months.

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

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**Post-ACTH serum cortisol**

- **<1.5 µg/dL (<40 nmol/L)** and clinically well
- **RETURN TO DAY 1**

- **1.5–6.0 µg/dL (40–165 nmol/L)**
- Continue on current dose, but monitor clinical signs carefully for recurrence.

- **6.0–9.0 µg/dL (165–250 nmol/L)**
- Continue monitoring with history, physical exam, chemistry panel, electrolytes and ACTH stimulation test every 3 months.

- **>9.0 µg/dL (>250 nmol/L)**
- Contact the manufacturer for advice on dosing.