

Melissa Herrera, DVM, Diplomate ACVIM, and Richard W. Nelson, DVM, Diplomate ACVIM, University of California–Davis

Do These Dogs Have Cushing's Disease?

Case 1

History. A 12-year-old neutered male miniature schnauzer presents for a routine geriatric wellness examination. The dog has had a good appetite and activity level; there are no reports of polyuria, polydipsia, or polyphagia. The owner reports that the dog has had increasingly severe “bad breath” and that the dog recently prefers canned food over his normal dry food.

Physical Examination. The dog is quiet, alert, responsive, and hydrated. Body weight is 9.2 kg, and body condition score is 4–5/9. The only abnormalities are severe halitosis, severe dental calculus, and moderate gingivitis. The dog rejects a complete oral exam and appears to be in pain.

Diagnostics. In preparation for general anesthesia and a dental prophylaxis with or without dental extractions, routine blood and urine tests are performed. Given the elevated ALP level, an ACTH stimulation test is performed. **Table 1** provides all laboratory results.

CASE 1: ASK YOURSELF ...

- Does this dog have Cushing's disease based on the results of the tests performed?
- What is your treatment plan?
- Would there have been a preferable diagnostic plan for this dog?



Case 2

History. An 11-year-old spayed female Labrador retriever (**Figure 1**) presents for evaluation of increased water intake and inappropriate urination in the house. The dog spends most of her time indoors, and over the last few months she has started to urinate excessively in the house. Her appetite is great (she has had a ravenous appetite since she was a puppy), but her activity is somewhat decreased. The owner attributes this to older age.

Physical Examination. The dog is bright, alert, responsive, and hydrated. Body weight is 28 kg, and body condition score is 5/9. Abnormalities consist of moderate muscle atrophy, especially of the hindlimbs, a mild “pot-bellied” appearance, and thin skin.

Diagnostics. Given the history, clinical signs, physical examination findings, elevated ALP level, hypercholesterolemia, and hyposthenuria, the primary differential diagnosis is hyperadrenocorticism. An ACTH stimulation test is performed; all test results are provided in **Table 1**.

CASE 2: ASK YOURSELF ...

- Does this dog have Cushing's disease? If so, how do you interpret the results of the ACTH stimulation test?
- What is your diagnostic and treatment plan?
- Would there have been a preferable screening test for Cushing's disease in this dog?

ACTH = adrenocorticotropic hormone; ALP = alkaline phosphatase

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Table 1. Laboratory Results

Variable	Case 1 Results	Case 2 Results	Reference Interval
Complete Blood Count			
Red blood cells (10 ⁶ /mCL)	5.39	7.17	5.6–8
Hematocrit (%)	38.9	43.6	40–55
White blood cells (10 ³ /mCL)	16.85	7.66	6–13
Neutrophils (10 ³ /mCL)	15.18	6.281	3–10.5
Bands (cells/mCL)	495	n/a	n/a
Lymphocytes (cells/mCL)	330	613	1000–4000
Monocytes (cells/mCL)	495	613	150–1200
Eosinophils (cells/mCL)	77	77	0–1500
Basophils (cells/mCL)	0	0	0–50
Platelets (10 ³ /mCL)	285	399	150–400
Urinalysis			
Urine specific gravity	1.028	1.008	n/a
Protein	Negative	1+	Negative
Glucose	Negative	Negative	Negative
Ketones	Negative	Negative	Negative
Bilirubin	Negative	Negative	Negative
White blood cells	0–2/hpf	0–2/hpf	0–2/hpf
Red blood cells	0–2/hpf	0–2/hpf	0–2/hpf
Bacteria	None seen	None seen	None
Urine Culture	Negative	Negative	Negative
ACTH Stimulation Test			
Pre-ACTH cortisol level (mcg/dL)	3.8	2.4	0–6
Post-ACTH cortisol level (mcg/dL)	22.6	13.8	6–15
Serum Biochemical Profile			
Sodium (mmol/L)	148	145	145–154
Potassium (mmol/L)	4.9	4.5	3.6–5.3
Chloride (mmol/L)	110	107	108–118
Total carbon dioxide (mmol/L)	21	24	16–26
Calcium (mg/dL)	10.2	11	9.7–11.5
Phosphorus (mg/dL)	4.8	4.7	3–6.2
Blood urea nitrogen (mg/dL)	18	11	5–21
Creatinine (mg/dL)	1	0.7	0.3–1.2
Glucose (mg/dL)	101	122	64–123
Total protein (g/dL)	7	6.9	5.4–7.6
Albumin (g/dL)	4	3.5	3–4.4
Globulin (g/dL)	3	3.4	1.8–3.9
ALT (IU/L)	78	95	19–67
AST (IU/L)	40	44	19–42
ALP (IU/L)	536	283	21–170
Total bilirubin (mg/dL)	0.1	0.1	0–0.2
Cholesterol (mg/dL)	298	399	135–361
Creatine kinase (IU/L)	111	92	51–399
GGT (IU/L)	< 3	< 3	0–6

Diagnoses

Case 1

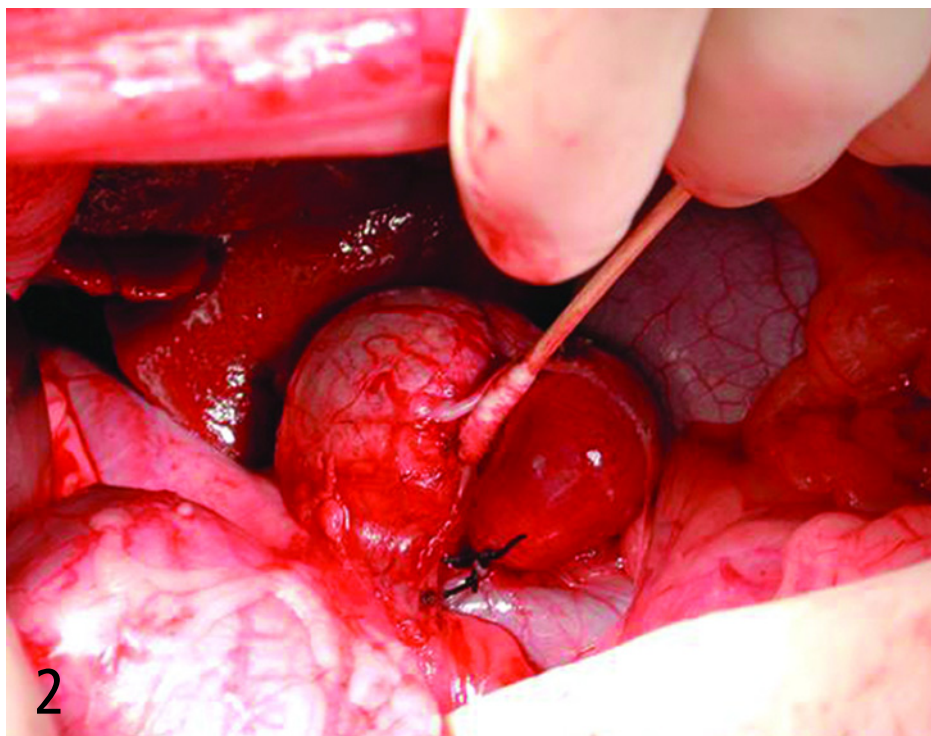
Cushing's disease should be considered only in dogs with appropriate historical and physical examination findings. This dog does not have any historical or clinical signs consistent with Cushing's disease. The elevated ALP level can be due to various isoenzymes; by itself, it is not a reason to investigate for Cushing's disease.

Improper investigation may lead to confusion, as illustrated in this example. The ACTH stimulation test may be considered consistent with Cushing's disease; however, because of the lack of appropriate historical and clinical signs, the elevated post-ACTH cortisol level is misleading.

There are 2 possible approaches for this dog: 1) pursue the indicated dental procedure and reevaluate the liver enzymes at a later date, or 2) pursue diagnosis of Cushing's disease or evaluation of the liver before performing the dental procedure. The decision is often based on the veterinarian's index of suspicion for Cushing's disease. In this dog, abdominal ultrasonography was performed, and the findings were unremarkable. The adrenal glands were normal in size and shape. This dog underwent a periodontal treatment along with extractions and will return for a liver panel in a month.

CASE 1: DID YOU ANSWER...

- No. The ACTH stimulation test is not warranted in this scenario because there are no historical or clinical signs suggestive of Cushing's disease.
- Pursue treatment of dental disease. Imaging (ie, abdominal ultrasonography) should be considered before anesthesia in this older patient, although treatment need not be delayed if the dental disease is believed to require immediate attention.
- Although not recommended in this scenario, a urine cortisol:creatinine ratio or a low-dose dexamethasone suppression test would have been the preferred screening test for Cushing's disease.



Blunt dissection of the right adrenal tumor during adrenalectomy

Case 2

In this dog, the muscle weakness and atrophy, “pot belly,” thin skin, and marked polyuria and polydipsia were indicators for suspicion of Cushing’s disease. Other top differential diagnoses for polyuria and polydipsia (eg, hypercalcemia, diabetes mellitus, pyelonephritis) were ruled out on the basis of blood and urine tests.

An ACTH stimulation test has lower sensitivity for Cushing’s disease compared with the low-dose dexamethasone suppression test. In this case, it would be preferable to perform the latter. The results of the low-dose dexamethasone suppression test (**Table 2**) are consistent with Cushing’s disease. However, pituitary-dependent hyperadrenocorticism and adrenal-dependent hyperadrenocorticism cannot be differentiated with these results because cortisol secretion was not suppressed.

Abdominal ultrasonography revealed a large right-sided adrenal mass with the contralateral adrenal gland at the low limits of normal size. Approximately 40% of dogs with hyperadrenocorticism caused by functioning adrenocortical tumors have ACTH stimulation test results within reference limits. Another consideration would be secretion of a different adrenal steroid (eg, 17 α -OH progesterone).

This patient successfully underwent right-sided adrenalectomy (**Figure 2**) and histopathology revealed a cortical adenocarcinoma. ■

See **Aids & Resources, back page, for references, contacts, and appendices.**
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ACTH = adrenocorticotropic hormone; ALP = alkaline phosphatase; ALT = alanine aminotransferase; AST = aspartate aminotransferase; GGT = gamma-glutamyl transferase; hpf = high-power field

Table 2. Low-Dose Dexamethasone Test Results: Case 2

Cortisol Level	Result	Reference Interval
Before testing (mcg/dL)	3.4	(0–6)
4 H after testing	2.9	(< 0.8)
8 H after testing	3.2	(< 0.8)

CASE 2: DID YOU ANSWER...

- Yes. Cushing’s disease is still the primary differential diagnosis in this patient. The ACTH-stimulation test result is false-negative because the patient has adrenal-dependent Cushing’s disease. The tumor cells are autonomously releasing cortisol regardless of the ACTH result.
- A low-dose dexamethasone suppression test and abdominal ultrasonography, with or without an endogenous ACTH stimulation test to verify a cortisol-secreting adrenal tumor, should be performed, followed by an adrenalectomy by an experienced surgeon at a hospital able to provide superb perioperative management. It would be reasonable to consider short-term medical treatment with trilostane for Cushing’s disease to decrease the endogenous cortisol. This treatment may help reduce surgical and postsurgical complications.
- A low-dose dexamethasone suppression test would have been the preferred screening test for Cushing’s disease. An ACTH stimulation test can lead to false-negative results, especially if the Cushing’s disease is adrenal dependent. As in the dog in this case, approximately 45% to 50% of dogs with functioning adrenocortical tumors weigh more than 20 kg.