

UNDERSTANDING CUSHING'S DISEASE IN DOGS

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Cushing's disease is one of the more common endocrine diseases that affect dogs, but it rarely occurs in cats. Although it is not life threatening, its side effects often lead pet owners to consider euthanasia if control cannot be maintained.

Technically referred to as hyperadrenocorticism, Cushing's disease is an overproduction of cortisol (a naturally occurring steroid) by the adrenal gland. This occurs as a result of a tumor on either the pituitary or adrenal gland. Iatrogenic Cushing's disease is the presence of all the typical signs resulting from excessive steroid administration by a veterinarian or owner.

PATHOGENESIS

A tumor of the pituitary gland, which secretes adrenocorticotropic hormone (ACTH; also called corticotropin), causes the adrenal gland to secrete excessive cortisol independent of the cortisol level in the blood.

Pituitary tumor =
↑ ACTH secretion = ↑ cortisol

Similarly, a tumor of the adrenal gland may cause the gland to secrete excessive cortisol independent of the ACTH level in the blood:

Adrenal tumor =
↑ cortisol despite ↓ ACTH

The net result is the same – an increased cortisol level in the blood – because the normal feedback mechanism has been bypassed. The many complex effects of increased cortisol on the body result in specific clinical signs.

CLINICAL SIGNS

Signs commonly associated with Cushing's disease include the following:

- **Polyuria and polydipsia**
- **Thinning of the skin and haircoat** (often with symmetrical hair loss)
- **Increased susceptibility to infections** (particularly of the skin and urinary tract)
- **Muscle weakness**
- **Pot-bellied appearance** from muscle weakness
- **Polyphagia**

All of these signs are secondary to elevated blood levels of cortisol.

DIAGNOSIS

The following three tests are commonly used to diagnose hyperadrenocorticism.

Urine Cortisol:Creatinine Ratio

A urine sample is analyzed to determine the urine cortisol:creatinine ration. If the cortisol level is above a given number when compared with the creatinine level the patient is likely to have Cushing's disease.

Because this test has a very low false-negative rate, a negative test can be assumed to be truly negative. IF the test is positive, one of the two tests below should be conducted to confirm the diagnosis.



Low-Dose Dexamethasone Suppression Test

For the low-dose dexamethasone suppression (LDDS) test, a baseline sample of the dog's blood is obtained. Then, a very small dose of steroid is administered intravenously, and two more blood samples are obtained at 4 and 8 hours after injection. Cortisol levels are measured in each of the three samples. In a normal dog whose feedback mechanism is intact, the small dose of dexamethasone given by injection will cause the pituitary gland to decrease its output of ACTH. Consequently, the adrenal gland will decrease its output of cortisol and the serum cortisol level will drop. This level should remain low at 8 hours after the steroid injection. Remember that dogs that have adrenal or pituitary tumors lose the feedback mechanism and their cortisol levels will not drop as low as expected, if at all. Dogs that initially suppress at 4 hours but rebound to a higher level at the 8 hour sample generally have a pituitary tumor.

To differentiate between a pituitary and adrenal tumor, a high-dose dexamethasone suppression test is available. The technique is the same as for a low-dose dexamethasone, a dog with adrenal-dependent hyperadrenocorticism will not suppress at either 4 or 8 hours after administration. A dog with

pituitary-dependent hyperadrenocorticism will typically suppress at both 4 – 8 hours.

ACTH Response Test

A blood sample is obtained to measure the animal's baseline cortisol level. A dose of ACTH is then administered and a subsequent blood sample is drawn to evaluate the cortisol level. An exaggerated elevation of the cortisol level after administering ACTH is usually diagnostic of Cushing's disease.

TREATMENT

Several medications are available for controlling Cushing's disease. Mitotane, the most commonly used drug, works by chemically destroying the cortisol-secreting portion of the adrenal gland. As a result, the blood level of cortisol drops and signs temporarily subside. Ketoconazole, an antifungal drug, has been used to successfully decrease cortisol output associated with Cushing's disease.

Because the underlying cause of the disease is a tumor, none of the medications is considered curative. They can, however, significantly decrease the blood level of cortisol and help maintain a good quality of life for an extended period. Treated dogs are monitored with an ACTH response test. Ideally, ACTH response tests are conducted 7 to 10 days after beginning medication and then at 1, 3, 6, and 12 months and every 6 to 12 months thereafter. However, this regimen is rarely followed in practice. More commonly, the test is scheduled after evaluating the patient's response to therapy and is based on the veterinarian's clinical experience.

In cases of adrenal tumor, surgical removal of the affected adrenal gland can sometimes effect a cure. On the other hand, pituitary tumor removal is difficult, dangerous and extremely expensive.

When hyperadrenocorticism is present in conjunction with diabetes mellitus, both diseases can be especially more difficult to control than usual. The presence of both of these conditions is neither common nor rare but should always be considered by the clinician. Because glucocorticoids, such as cortisol, affect glucose metabolism and insulin efficiency, uncontrolled cortisol output associated with hyperadrenocorticism makes regulation of blood glucose especially difficult. In a clinical situation, the best option is to attempt to control the Cushing's disease first, then attempt to regulate the diabetes.

