

## **What Exactly is Cushing's Disease**

**By Wendy C. Brooks DVM, DABVP**

Cushing's Syndrome is the resulting set of symptoms observed when the body is exposed to excess cortisone (or related hormones) over a long period of time. Cortisone, or more correctly "Cortisol," is a hormone produced by the adrenal glands which are located atop the kidneys. Cortisol is stored in the adrenal gland and released in times of stress where it helps our bodies prepare for a "fight or flight" situation. It adjusts the metabolism to expect physical exertion by mobilizing fat and sugar stores and retaining sodium and water. It puts us in a state of "break down" so that our stored resources can be used quickly. If the body is exposed to this hormone most of the time instead of during short stressful periods, the state of break down becomes debilitating.

There are several mechanisms which can lead to Cushing's syndrome and, as they are treated differently, it is important to determine which one is at work in a given animal.

In the normal body, the pituitary gland, located at the base of the brain, can detect when cortisol levels in the blood are declining. In response, the pituitary secretes a stimulating substance which causes the adrenal gland to release more cortisol. When the pituitary gland detects that cortisol levels are again appropriate, it stops its stimulatory message.

You can think of the pituitary gland as a sort of a thermostat for cortisol. This raising and lowering of cortisol blood level is regulated throughout the day and occurs rapidly.

### **PITUITARY-DEPENDENT CUSHING'S SYNDROME**

This accounts for 85% of dogs with Cushing's syndrome. Basically, the pituitary gland grows a tumor, generally microscopic and generally benign. This tumor, however, over-produces its stimulatory message thus leading to enlargement of both adrenal glands and an over-production of cortisone. Occasionally (10% of pituitary-dependent Cushing's dogs), these benign pituitary tumors are large enough to compress the brain. In these cases, neurological signs may be observed; these cases are unusual but very hard to treat.

### **ADRENAL-DEPENDENT CUSHING'S SYNDROME**

In 15% of dogs with Cushing's syndrome, an adrenal tumor is directly over-producing cortisone. The tumor is often large enough to see with radiographs or ultrasound and may be malignant.

### **OVERUSE OF CORTISONE-TYPE HORMONES**

Cortisone derivatives may well be the most over-used drugs in veterinary medicine. Their anti-inflammatory actions soothes such common maladies as allergic skin disease (especially flea allergic dermatitis) and degenerative arthritis. Relief is usually rapid and many owners find themselves requesting "cortisone" shots or pills over and over again. In time, Cushing's syndrome results, not from any inherent disease in the pet's system but from the effects of the hormones given.

The pituitary gland perceives the high steroid levels yielded by the medication and does not send a stimulation to the adrenal glands. In time, the adrenal glands atrophy and are not able to release cortisone for a period of three months after the medication is discontinued. To allow the adrenal to gradually recover, cortisone pills are usually

prescribed in a decreasing dose and an owner should never discontinue the pills suddenly.

Commonly prescribed cortisone derivatives include: vetalog, azium, prednisone, prednisolone, dexamethasone, depomedrol and others.

*Date Published: 1/1/2001*

*Date Revised: 10/10/2005*

## **Hyperadrenocorticism (Cushing's Disease)**

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Healthy skin and a normal hair coat are the result of many factors, both external and internal. There are several glands in the body responsible for the production of hormones that are vital for the regulation of other body functions as well as a normal skin surface and hair coat.

Cushing's disease results from an overproduction of the hormone cortisol. Cortisol is produced by the adrenal glands (located next to the kidneys) and stimulated to produce cortisol by the pituitary gland (at the base of the brain). Disease may be due to overproduction in the adrenal glands by themselves or overstimulation of the adrenal glands by the pituitary gland.

Signs associated with Cushing's disease may include increased thirst and urination, a voracious appetite, an enlarged sagging belly, hair loss, lethargy/weakness, panting and sometimes recurrent infections. Without treatment most dogs will die within one or two years. With treatment your pet's life can be prolonged, at times to a normal life span. Treatment consists of medication to control the overproduction of cortisol by the adrenal gland or surgery to remove the abnormal adrenal gland. Which treatment is best depends upon where the problem is in the dog's body (pituitary or adrenal).

### **Diagnosis**

Cushing's disease can be difficult to diagnose, especially in early cases. Tests that may be needed may include: a complete blood count, chemistry panel, urinalysis, ACTH stimulation test (a 1- or 2-hour test), low dose dexamethasone suppression test (an 8-hour test), a high dose dexamethasone suppression test (an 8-hour test), an ACTH assay, radiographs or CT scan, and possibly other tests!

### **Testing: Confirming Cushing's Syndrome**

**By Wendy C. Brooks DVM, DABVP - Diagnosis of Dogs**

#### ***The Low Dose Dexamethasone Suppression Test***

Dexamethasone is a cortisone-type hormone which is used therapeutically for numerous conditions. The dog's pituitary gland will perceive the presence of dexamethasone and shut off its stimulatory message to the adrenal glands. In the normal animal, this means

that a drop in blood cortisol level will be seen 8 hours after a tiny dose of dexamethasone is given.

If a pituitary tumor is present, the pituitary is not about to shut off its stimulatory message and ignores the presence of the dexamethasone. No drop in cortisol level is seen at the end of eight hours.

***THIS TEST IS CURRENTLY CONSIDERED THE MOST ACCURATE IN THE CONFIRMATION OF CUSHING'S DISEASE.***

***To Run This Test***

Ideally this test is run in the morning. A baseline cortisol level is measured, a low dose of dexamethasone is given intravenously, and blood samples are checked again in 8 hours. Sometimes a 4 hour sample is also drawn as the pattern of suppression over the entire 8 hours may help classify the type of Cushing's disease. The pet will require at least 8 hours in the hospital.

***The ACTH Stim Test***

Central to the concept of Cushing's disease is the over-production of cortisol. It follows then that the adrenal glands of the Cushing's patient would possess large amounts of stored hormone due to their chronic stimulation.

We have been talking about the stimulatory message sent from the pituitary gland to the adrenal glands. This message consists of a hormone called "***Adrenocorticotrophic hormone***" or "***ACTH***." In this test, a dose of ACTH is given to the patient. If a larger than expected, rise in cortisol levels is measured in 2 hours we may diagnose Cushing's syndrome.

***To Run This Test***

Ideally, the patient is fasted overnight and the test is performed in the morning between 8 A.M. and 10 A.M. A blood sample is drawn, a dose of ACTH is given, and two hours later a second blood sample is drawn.

***When Would We Run this Test?***

Given that the Low Dose Dexamethasone Suppression test is more accurate, when might we run this test instead? It turns out that this is the only test that can be used if the ***iatrogenic form of Cushing's disease*** is suspected. This test is also crucial in monitoring patients with Cushing's disease, depending on which medications are used.

***The Urine Cortisol:Creatinine Ratio***

This is a screening test for Cushing's disease; a positive test here does NOT confirm Cushing's syndrome but a negative test here DOES rule it out. In this test a single urine sample is collected and the relative amounts of cortisol and creatinine (creatinine is a protein metabolite that is excreted in urine constantly). If there is a high ratio (a relatively high amount of cortisol being excreted), further testing is in order.

***Diagnosis of Cats***

In cats, the tests that are reliable in dogs simply are not helpful. The ACTH stim test produces unacceptable false negatives and false positives. The Low Dose

Dexamethasone Suppression Test cannot be performed using the same dexamethasone dosing as in dogs. (Instead the doses used for the High Dose Dexamethasone Suppression Test in dogs can be used in the Low Dose Dexamethasone Suppression Test for cats). This test will pick up most feline cases of Cushing's disease but it turns out the most reliable feline test is the least reliable canine test: the urine cortisol:creatinine ratio. To perform this test, the owner will need to bring in a urine sample obtained in the morning. This can be most easily done by covering the litter box with clear plastic food wrap (the cat will urinate on the wrap and the urine can be collected). Alternatively, the box can be cleaned and only a small amount of litter placed inside (the urine can be collected from the bottom of the box - a few specks of litter in the sample will not matter). There is also a product called "No Sorb" litter that is made of plastic beads. It can be cleaned and re-used and your veterinarian's office may send home this or a similar product to assist with urine collection.

A total of two samples from consecutive days are needed. After the second day, a discrimination test to determine the type of Cushing's disease is performed. The cat is given oral dexamethasone tablets to take at 8-hour intervals (8 AM, 4 PM and midnight would be a typical schedule) and a third urine sample is brought to the vet's office. At the end of this testing, the veterinarian will know whether the cat has Cushing's disease and will have a sense of whether it is the adrenal or pituitary form. Assuming the cat has Cushing's disease, there is one last diagnostic test and that is ultrasound. The ultrasound results must match the results of the dexamethasone suppression test. The cat will be ready for treatment once the type of Cushing's disease has been determined.

Date Published: 1/1/2001