

# The Animal Medical Clinic

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## Cushing's Disease in Dogs (Hyperadrenocorticism)

Cushing's Disease is a disorder in which the adrenal glands overproduce certain hormones. Another medical term disease for this disease is *hyperadrenocorticism*. There are two adrenal glands, one on each side of the abdomen; they are located just above each kidney.

The adrenal gland is divided into two layers: an outer cortex and inner medulla.

**Medulla.** The medulla produces hormones that help the dog respond to stress, regulate metabolism and maintain the tone of blood vessels. The most significant medullary hormone is adrenaline (epinephrine).

**Cortex.** The adrenal cortex is comprised of three layers, each with an important function. Some of these functions include regulation of sodium and potassium balance and production of steroid hormones. Some of these steroid hormones, such as glucocorticoids, are essential for sustaining life. The most well known glucocorticoid is cortisol (or cortisone).

### Prevalence

Spontaneous Cushing's is common in dogs over 6 years of age. The average age of onset is approximately ten years of age.

For pituitary-dependent Cushing's (PDH), as described below, there are breeds which have an increased incidence of the disease. These breeds include all Poodle breeds, German Shepherd dogs, Beagles, Labrador Retrievers, Dachshunds, Boxers, and some Terrier breeds, including Boston Terriers. It occurs with equal frequency in male and female dogs.

For adrenal-dependent Cushing's (ADH), as described below, the disease is more common in female dogs and in the larger breeds. These breeds which appear most often affected with ADH include Poodles, German Shepherd dogs, Dachshunds, Labrador Retrievers, and terriers.

### Causes/Transmission

There are three mechanisms by which this disease can occur. Regardless of the cause, the clinical signs are essentially the same. It is important to identify the cause, however, because the various forms are treated differently and have different prognoses.

**Iatrogenic.** Iatrogenic Cushing's Disease means that the excess of cortisone has resulted from excessive administration of a cortisone-containing drug. This may occur from oral or injectable medications. Although the injections or tablets are given for a legitimate medical reason, excess can be detrimental.

**Pituitary gland tumor (PDH).** The most common cause of Cushing's Disease (80 - 85% of all cases) is a benign tumor of the pituitary gland; it is rare for these tumors to be malignant. The tumor causes the pituitary to overproduce a hormone that, in turn, stimulates the adrenal glands. Excessive cortisone secretion results. The tumor

may be either microscopic (called a *microadenoma*) or quite large (called a *macroadenoma*). Depending on the size of the tumor, the presence of signs other than Cushing's will be variable. It is hoped that if the activity of the adrenal gland can be controlled, the dog will live a relatively normal life. Unfortunately, this is not always the case. However, many dogs with this form of Cushing's Disease can live normal lives for many years if they take their medication and stay under close medical supervision. Growth of the pituitary tumor would give the patient a less favorable prognosis.

**Adrenal gland tumor (ADH).** In 15-20% of cases, Cushing's Disease is the result of a benign or malignant tumor of the adrenal gland. If benign, surgical removal cures the disease. If malignant, surgery may help for a while, but the prognosis is less favorable than for a benign tumor.

### **Clinical Signs**

The most commonly reported clinical signs associated with Cushing's Disease are a tremendous increase in appetite, water consumption, and urination. Lethargy (lack of activity), panting, and muscular weakness are also seen in many cases. Problems related to the skin and hair coat include thin, easily bruised skin, loss of hair (alopecia), and excessive pigmentation.

Many of these dogs appear to have a bloated abdomen. There are two primary causes for this. The liver grows quite large with all types of Cushing's; this enlargement is called *hepatomegaly*. At the same time, the muscles of the abdomen are weaker and unable to adequately support the liver. With time, the dog develops a very pendulous-looking abdomen.

Occasionally, neurologic signs are seen. These signs include but are not limited to seizures, altered behavior, and incoordination.

### **Diagnosis**

A number of tests are necessary to diagnose and confirm Cushing's Disease. The most common initial tests are either the ACTH stimulation test or the low-dose dexamethasone suppression test. These tests are used to confirm that the dog has Cushing's.

Frequently, additional tests are needed to discriminate between the various forms of Cushing's (PDH vs. ADH). The main discriminatory tests are called the high-dose dexamethasone test and the ACTH assay.

### **Treatment**

**Iatrogenic Cushing's Disease.** Treatment of this form requires discontinuation of the cortisone-containing medication. This must be done in a very controlled manner so that side-effects do not occur from withdrawal of the drug. When a prolonged course of cortisone therapy is necessary, the adrenal glands will atrophy and need time to "relearn" their normal functions. Unfortunately, stopping the cortisone can result in recurrence of the disease that was being treated by the cortisone. Because there may have been adverse effects on the adrenal glands, treatment is also needed to correct that problem.

**Pituitary Tumor** Treatment of PDH is designed to destroy the part of the adrenal cortex so that excessive cortisone will no longer be produced. The drug, Lysodren™, is used to destroy the adrenal tissue. Lysodren™ is also known as mitotane or o'p'-ddd. If not enough drug is used, the abnormal tissue persists and the disease continues. If too much is used, most or all of the adrenal cortex will be destroyed, which can be life threatening. Therefore, careful monitoring of the dog is necessary in order to achieve good results. Because the pituitary is not being affected by the treatment, it continues to stimulate the adrenal gland. This means that continued treatment is necessary. Although a cure is not achieved, control is possible for many years if the tumor is small. If the tumor is large, local effects of the tumor invading surrounding tissues in the head can be the limiting factor in survival. A newer therapy has become available within the past two years. The drug, called Anipryl™, does not offer the dramatic improvement more typically seen with Lysodren™, but is safer. It is relatively expensive and is only useful for the pituitary-dependent form of Cushing's.

**Adrenal Tumor** Treatment of an adrenal tumor requires treatment with Lysodren™ and/or major surgery. With some adrenal tumors, especially the benign form (adenoma), good results can be achieved with drug therapy alone. In some cases, surgery is indicated for purposes of obtaining a biopsy and/or attempting to remove the tumor mass. This surgery is potentially very dangerous to the dog, even when performed by skilled surgeons, because the tumor is typically surrounded by large blood vessels.

### **Prognosis**

Dogs with ADH caused by a benign tumor have a good prognosis whereas the prognosis is guarded with the malignant form (adenocarcinoma). The prognosis with PDH is variable depending upon whether the tumor is a small tumor (microadenoma) or large tumor (macroadenoma), presence of concurrent medical problems, and willingness of the owner to continue with treatment and monitoring.

### **Maintenance Phase**

When regulated, your dog will take Lysodren™ approximately once weekly. An ACTH stimulation test will be necessary about every 3-4 months to be sure that regulation is satisfactory. At the appropriate time, the specifics of the maintenance phase will be explained.