

## HYPERADRENOCORTICISM "CUSHING'S DISEASE"

Cushing's Disease was named after Harvey Cushing, the physician who first described the disease in people at the turn of the century. The technical name of Cushing's Disease, hyperadrenocorticism, is easier to understand if it is broken down into its component parts. The adrenal glands are located on each side of the body just in front of each kidney. The outer layer of these small glands, called the cortex, produces hormones called corticosteroids - the body's own cortisone-like chemicals. The corticosteroid that we measure with blood testing is called cortisol.

The inner layer of the adrenal glands, called the medulla, produces a set of hormones called mineralocorticoids, which regulate sodium and potassium levels in the body.

In hyperadrenocorticism, the adrenal glands produce excessive amounts of adrenal hormones. The excess hormones in the body lead to the symptoms of the disease - excessive urination and water drinking, thin skin and haircoat, liver swelling, muscle weakness often leading to a pot-bellied appearance, panting, obesity, frequent infections, especially of the skin or urinary tract. Signs progress slowly but surely, creating more and more problems as time goes on.

These symptoms may not all occur at once. Many times in the early stages Cushing's Disease resembles many other disease problems. The diagnosis may be suggested by changes in blood chemistry tests, which also help diagnose other diseases which can cause similar symptoms.

There are two causes of the disease. The first is a tumor of an adrenal gland. This tumor consists of excess glandular tissue which simply produces too much of its normal hormone. Adrenal tumors can be benign (non-cancerous) or malignant (cancerous).

More commonly (80-85% of the time) the tumor causing the problem is in the pituitary gland at the base of the brain. The pituitary responds to changes in the body such as stress, day length exposure, disease and other factors, and releases a hormone called adrenocorticotrophic hormone, or ACTH, into the bloodstream. ACTH stimulates the adrenal glands to produce cortisol. In a normal dog or person, the pituitary sends an appropriate amount of ACTH into the system to produce the proper amount of cortisol to maintain health. A pituitary tumor produces too much ACTH, which stimulates the adrenal gland to produce too much cortisol.

Pituitary tumors can also be benign or malignant. Benign ones tend to grow very slowly, causing no problems for years other than the effects on the adrenal glands. Malignant tumors may cause trouble much sooner, but these are rare. Whether benign or malignant, if the tumor becomes large enough it will eventually damage other tissues in the brain and neurological symptoms will start to occur - seizures, blindness or behavior changes.

There are several specific test protocols that are used to diagnose Cushing's Disease and to determine which type of disease, pituitary dependant or adrenal, a dog has. They all involve testing cortisol levels before and after the administration of other hormones, to see if the adrenal and pituitary glands respond appropriately. An ultrasound scan of the abdomen can also be done to look for adrenal tumors. A urine test called a cortisol/creatinine ratio can be used as a screening test for Cushing's disease as well. This can be a difficult disease to diagnose and

sometimes multiple tests are needed.

Adrenal tumors can be surgically removed. If only a single gland is involved, the other one will take over cortisol production after surgery and the symptoms of Cushing's Disease will go away. Sometimes the opposite adrenal gland will eventually develop a tumor as well. This is especially common in ferrets but is rare in dogs and cats.

Pituitary tumors are located too deep in the brain to surgically remove. Therefore, the treatment for the 85% of patients who have this form of the disease is medical, not surgical. There are two medications available. The newest, called Anipryl, is much safer than the older medication we used to use so it is usually our first choice. It decreases the amount of ACTH produced by the pituitary gland. Given once daily, symptoms usually begin to improve within a month. Periodic retesting may be needed to monitor the disease. Anipryl is fairly expensive, costing \$40-60 per month and it doesn't work in every dog. If we don't see good results we switch to the other drug.

The older medication, called Lysodren, is less expensive and sometimes more effective but also has greater risk. It destroys adrenal tissue so that there is less adrenal gland left to produce cortisol. Even though the pituitary is still producing too much ACTH, there isn't enough adrenal tissue left to respond. The hard part is getting the right dosage of this medication to destroy just enough adrenal tissue but not too much. One or two doses too many can destroy so much adrenal tissue that mineralocorticoid production is affected. When this happens the sodium and potassium balance is disrupted. Vomiting, heart rhythm disturbances, collapse and even death can result. Emergency IV saline treatment is necessary if sodium levels become too low. Close monitoring is needed when using this medication.

Often oral supplements of the mineralocorticoids are needed after treatment with Lysodren - sometimes temporarily, sometimes for life. Often supplements of corticosteroid hormones are needed as well, at least for the first few days after the initial Lysodren therapy.

The dog receives Lysodren twice daily until adrenal production drops. As soon as production starts to resume, a weekly dosage of Lysodren is initiated to maintain control. Periodic testing for adrenal function assures good control of the disease. Unless the tumor causing the disease is one that can be removed, treatment is lifelong. Although most do well, again there can be serious side effects in a few dogs.

As you might guess, the cost of diagnosis and treatment vary greatly depending on the dog. Diagnosis alone can cost well over \$300 in some cases. The medications are expensive. With Lysodren treatment, there is no way we can predict whether your pet will need medication for 3 days or for the rest of its life. If emergency treatment is needed for electrolyte disturbances, that may be several hundred dollars. Whichever drug or treatment is used, regular recheck blood tests will be needed to monitor the course of the disease.

If your dog does well on Anipryl or Lysodren the prognosis is good. The average lifespan after diagnosis is about two and one half years, but we have several patients who have done well on their medication for more than 5 years. Hyperadrenocorticism IS considered a life-shortening disease, and some dogs will do much better than others. Since the disease usually occurs in middle to aged or older animals, there may also be complications due to other organ dysfunction.

Please let us know if you have any questions about this disease. We want to make sure you understand it before making a decision as to treatment for your pet.

