

HYPERADRENOCORTICISM OR "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.

In hyperadrenocorticism, the adrenal glands produce excessive (hyper) amounts of adrenal cortical hormones (cortisols). The excess hormones in the body lead to the symptoms of the disease - excessive urination and water drinking, voracious appetite, thin skin and haircoat, liver swelling, muscle weakness often leading to a pot-bellied appearance, panting, obesity and 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.

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. This second type of hormone becomes important when we begin treating for Cushing's disease.

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 gland is supposed to respond to changes in the body such as stress, day length exposure, disease and other factors, and it releases a hormone called adreno-corticotrophic hormone, or ACTH, into the bloodstream in response to these factors. 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, in contrast, produces too much ACTH, which stimulates the adrenal glands 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

Caring People Helping Pets



2082 Cheyenne Court, Grafton, WI 53024 • phone: 262-375-0130 • fax: 262-375-4196 • www.bestfriendsvet.com



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 test is the least expensive. It's great to rule out Cushing's – if it's negative it's unlikely the dog has the disease – but we get a lot of false positives on this test. Stress increases cortisol levels and can cause false positives on all of the tests. This can be a difficult disease to diagnose, especially if the pet has other stressful or serious health problems, and sometimes multiple tests are needed.

Adrenal tumors can be surgically removed. If only a single adrenal gland is involved and removed, 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 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 Cushing's patients who have this form of the disease is medical, not surgical. Cushing's disease develops slowly, with symptoms gradually growing worse over time. Treatment for it is expensive and has risks associated with it. We generally do not recommend treatment until the symptoms warrant the risk and the cost. Regardless of the results of the blood tests if a dog does not have symptoms that are causing problems for the pet or the owner, we don't treat it.

There are two medications available. Selegiline is much safer than the other medication but is only effective in about 20% of dogs. It decreases the amount of ACTH produced by the pituitary gland. Given once daily, symptoms would begin to improve within a month. If it is helping it would then be used for the remainder of the pet's life. Periodic retesting would be needed to monitor the disease. Selegiline is available as a human generic, so the cost is quite reasonable. It's worth a try before moving on to more expensive therapies.

The other option is a drug called trilostane (Vetoryl®). It comes in several different sizes of capsules and is administered daily. It is about 85% effective – a few dogs will not respond to it. Trilostane's main drawback is its expense, including the monitoring needed after starting on it. If your dog is diagnosed with Cushing's disease we will get you a current price for the size you need but you can expect to pay hundreds of dollars a year – another reason we wait until symptoms are significant before beginning treatment.

Trilostane reduces the ability of the adrenal gland to make cortisol. Even though the pituitary tumor is still producing too much ACTH, the adrenal glands are not able to respond with excessive amounts of cortisol.

Side effects occur if too much of the drug is given. These include poor appetite, lethargy, weakness and dehydration. These symptoms would indicate that the cortisol level has dropped too low. If side effects occur the medication is temporarily discontinued and then resumed at a lower dose. Supportive care such as IV fluid therapy may be needed depending on the severity of symptoms. This drug should not be used in patients with severe liver or kidney disease. A rare but frightening side effect is adrenal gland necrosis in which the adrenal gland cells die, which is usually fatal. Thankfully it doesn't happen often but it's the reason we will very carefully monitor your dog's cortisol levels once he or she is taking the medication.

Periodic testing for adrenal function assures good control of the disease. These are "ACTH stim tests" where we inject a drug to stimulate the adrenal glands and then test the cortisol level 1 hour later. Unless the tumor causing the disease is one that can be removed, treatment and monitoring are lifelong. Although most dogs do well, again there can be serious side effects in a few dogs.

The cost of diagnosis and treatment vary greatly depending on the dog and the size of the dog. Diagnosis alone can cost well over \$1000 in some cases. The medications are expensive. If emergency treatment is needed for side effects, that also may be several hundred dollars or more. 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 whatever medication is chosen 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, however, and some dogs will do much better than others. Since the disease usually occurs in middle aged or older animals, there may also be complications due to other organ dysfunction.

If pituitary Cushing's disease is not treated, symptoms usually gradually worsen with time. Severe skin inflammation as in the pictures below, liver dysfunction, strokes due to high blood pressure, recurrent urinary tract infections and tremendous excessive urination are all possible. Many older dogs with mild Cushing's don't live long enough to develop all these symptoms and die of something else with their Cushing's symptoms still very mild. Dogs that are diagnosed when they are middle aged have more time for serious signs to develop. We generally sit down and have a conversation about risks, benefits and costs of treatment, to decide whether to treat and when.

Cushing's caused by an adrenal tumor can develop serious symptoms much earlier on. Adrenal tumors are generally much faster growing and cancerous than pituitary tumors. Time is of the essence if surgical removal is to be curative, which is why we push you to do the diagnostic testing early on to know for sure which type we are dealing with.

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.

The top row of pictures below shows the usual progression of Cushing's disease. The coat gets thinner and thinner, the skin becomes dry and thin like tissue paper and the abdomen begins to look distended. Not every case presents like this, however, and not all affected dogs are the typical small breeds. The bottom pictures are of a Labrador retriever who developed high blood pressure and a severe skin disease called calcinosis cutis due to Cushing's.

