ORANGE VILLA
VETERINARY HOSPITAL
BOARDING & GROOMING
714 - 637 - 3660

Dr. Richard E. Dahlem :
drdahlem@orangevillavet.com
Dr. Jeffrey Horn :
drhorn@orangevillavet.com
Dr. Sage:
drsage@orangevillavet.com

Cushing's disease

Cushing's disease is a syndrome in which there is an excessive amount of corticosteroids circulating in the body. Corticosteroids are hormones, which help the body to deal with stress. They are produced in the adrenal glands, which are located near the kidneys in the abdomen. Corticosteroids help to break down fat and sugars to aid the body with stressful situations. They are the opposite of the anabolic steroids that weightlifters use. Too high a level of corticosteroids for a long period of time causes severe illness. The technical term for Cushing's disease is hyperadrenocorticism and it occurs commonly in dogs and occasionally in cats.

Cushing's disease can be caused in two ways. One is from chronic administration of steroids by a veterinarian, which is called Iatrogeninc (veterinary-caused) Cushing's. Corticosteroids are used to relieve inflammation (from skin, ear, or eye disease or arthritis) or as an immune-suppressant for certain diseases. It is because of this risk of Cushing's Disease that we try to avoid chronic corticosteroid usage. Corticosteroids come in eye and ear medications, injections, and pill forms. Even topical medications can be systemically absorbed. Some examples of corticosteroids (also called glucocorticoids) used by veterinarians are:

- Prednisone, Prednisolone, Dexamethasone, Vetalog, Depo-medrol, Solu-deta-Cortef, Triamcinalone, Hydrocortisone, Betamethasone, Isoflupredone, Flumethasone, and Methylprednisone.

- These steroids can come mixed in other preparations: Synotic, Otomax, Triotic, Gentocin and Baytril Otic, BNP+Dex, Tresaderm, Tritop, Gentocin Spray, Gentocin Durafilm, Resicort, Panalog, and Dermalone.

The other way pets can have Cushing's Disease is if their own bodies produce too much corticosteroid in the adrenal gland. This steroid is called cortisol. There are two ways that this can occur. The most common cause is that a gland near the brain called the pituitary gland gets a microscopic benign tumor, which overproduces a hormone (ACTH), stimulating the adrenal glands to produce cortisol. Other than excessive cortisol levels, the tumor rarely causes other problems, although it can get big enough to press on the brain and cause neurologic problems. The other cause is an adrenal gland tumor. Luckily this is a rare condition.

What is the significance of Cushing's Disease? Cushing's disease causes many symptoms. Not all dogs have every symptom.

- Increased thirst and urination: the most common sign. A normal dog should drink

Dr. Richard E. Dahlem :
drdahlem@orangevillavet.com
Dr. Jeffrey Horn :
drhorn@orangevillavet.com

about a cup of water per ten pounds of body weight. This symptom can occur from many diseases (see the article on water in's and out's). Corticosteroids cause an increase in urination that causes the excessive thirst. Without adequate water, they can dehydrate easily.

- Excessive appetite: Cushing's Disease causes an increased to ravenous appetite. They beg, steal food, and will not lift their heads from the bowl until it's empty.

- Increased panting

- Muscle weakness and wasting

- Pot-bellied appearance: as muscle breaks down and abdominal fat increases, they get a large round belly

- Skin problems: Hair loss, especially along the body but not the head or legs is common. Due to immune suppression, skin infections (itching, skin crusts) are common. They can get darkening of the skin. Calcium build-up in the skin called calcinosis cutis can give them an Armadillo-like armor plate feel.

- High blood pressure

- Sudden acute blindness

- Lethargy

- Testicular atrophy and infertility in males and females

- Pancreatitis: a severe condition due to inflammation of the pancreas causing profuse vomiting and severe abdominal pain

- Urinary tract infection: immune suppression causes recurrent urinary tract infections

- Cats can get a curling to their ear tips and can develop diabetes mellitus

Dr. Richard E. Dahlem :
drdahlem@orangevillavet.com
Dr. Jeffrey Horn :
drhorn@orangevillavet.com

- Liver disease: The liver can accumulate large amounts of cortisol, causing liver problems including anorexia, vomiting, jaundice (icterus), or neurologic problems.

Is my dog at risk? Any animal on corticosteroid medication is at high risk for developing Cushing's Disease. The treatment would be to slowly withdraw the steroids and the problem will go away. Naturally occurring Cushing's Disease occurs in older dogs and cats as a general rule, although it can occur at any age. Breeds we see it most commonly in are Poodles, Dachshunds, Boston terriers, Boxers, and Beagles although any breed can be affected. Symptoms occur late in the disease and severity depends on length of course and levels of steroids in their systems.

How is Cushing's diagnosed? A careful history and physical examination can sometimes make us suspicious. Sometimes the pets are brought in for the symptoms, but the onset is so slow that the symptoms are missed, or thought to be from "old age." We frequently become suspicious due to abnormalities on a senior lab profile (blood and urine tests). This is one of the reasons that annual examinations and lab work are so important in older pets. Some changes that make us suspicious are:

- Increased white blood cell count, especially neutrophils and monocytes that are two types of white blood cells. Another type, called lymphocytes are sometimes decreased. This is called a "stress leukogram".

- Increased liver enzyme called alkaline phosphatase (ALP or ALKP). This is a liver enzyme. Liver enzymes increase with liver damage, but pets with Cushing's Disease can create a very similar enzyme, which appears the same on a blood panel. When this enzyme is elevated, we become suspicious of liver disease or Cushing's Disease.

- Elevated cholesterol: Cholesterol increases with many hormonal disorders and is a good indicator that something is amiss. Since most pets eat a much healthier diet than we due, this is a good indicator that something is wrong.

- Dilute urine

- Urinary tract infections, especially if they are recurrent

- Increased urinary cortisol: creatinine ratio: if there is a lot of cortisol in the body, it can dump into the bladder. Unfortunately, stress can cause this as well. A negative result

Dr. Richard E. Dahlem :
drdahlem@orangevillavet.com
Dr. Jeffrey Horn :
drhorn@orangevillavet.com

generally means that there is no Cushing's Disease, but a positive result does not mean that there is. Urine brought from home is better to test for this than urine obtained in the hospital. We generally run this routinely on older pets that have a history of excessive thirst or urination.

There are specialized tests that we use for Cushing's Disease. We like to use the most accurate and non-invasive tests to get a diagnosis. There are two ways we do this. One is blood testing, and the other is an imaging technique.

- One blood test is called the dexamethasone suppression test. Dexamethasone is a synthetic corticosteroid hormone. When the body has a certain amount of steroids circulating in the bloodstream, there is a negative feedback going to the pituitary gland (that gland near the brain). This feedback causes a decrease in the secretion of a hormone called ACTH that goes through the blood and causes the adrenal glands to produce cortisol. When dexamethasone is given injectably, the adrenal glands should stop producing cortisol for 8 hours. With the test, we draw some blood, give the injection, and we draw some blood at 4 hours and 8 hours after the injection. We then send the samples to the lab to measure cortisol levels. If the levels are higher than they should be, the pet has Cushing's Disease. This test is about 95% accurate in identifying Cushing's Disease if the pet has it. The test can also sometimes discriminate between Cushing's Disease due to a pituitary gland problem and an adrenal gland tumor. If we find out that the pet has Cushing's but we cannot tell whether it is an adrenal tumor or pituitary dependent, we may run other tests. We can repeat the dexamethasone suppression test at a higher dose or perform ultrasound.

- Another test is called an ACTH stimulation test. ACTH is the hormone secreted by the pituitary gland that stimulates the adrenal glands to produce cortisol. Overactive adrenal glands store excessive levels of cortisol. When ACTH is given as an injection, cortisol is released. Dogs with Cushing's disease release more cortisol than normal dogs do. To perform this test, we draw blood, give an injection of ACTH, and then draw blood again in 1 hour. The cortisol levels are then measured at the lab. The test is about 75% accurate in diagnosing Cushing's disease. Because it is not as accurate at the dexamethasone suppression test, we do not often use it for diagnosis. It is a good test to run if we are using medication Lysodren to treat the disease. This will be discussed later.

The other test is an imaging technique called ultrasound. If you want to learn more about ultrasound, look up our article on it. With ultrasound, we can look at the entire abdomen and can actually see the adrenal glands. We can use the ultrasound to compare the left and right adrenal glands and get measurements. If there is a tumor present, we can look for signs of spread or metastasis as well. It is non-invasive and non-painful. We do have to shave their bellies and some pet's require sedation if they won't hold still, but most don't require it.

Dr. Richard E. Dahlem :
drdahlem@orangevillavet.com
Dr. Jeffrey Horn :
drhorn@orangevillavet.com

What if my pet has Cushing's Disease? Pituitary-dependent Cushing's Disease is treated with medication. An adrenal gland tumor can be treated with medication for a while, but surgical removal is a better option. Surgery is pretty straight forward, so I will discuss the medical treatment. All medications are lifelong treatments.

- L-deprenyl (Anipryl) is the newest medication available. This drug, which is also used for certain types of senility in dogs, increases dopamine levels in the brain. Dopamine is a neurotransmitter, which in addition to other functions, inhibits secretion of ACTH (the hormone which travels to the adrenal glands). With decreased ACTH production, less cortisol is produced. So this drug attacks at the source of the problem. The medication's only major side effect is insomnia, so we give it in the morning. It is a once daily medication. To see if it is working, we monitor the pet's symptoms and we perform the dexamethasone suppression test. The drug does have two downsides. One is its cost. It is expensive. The other is that it is not effective in all dogs. If we see no improvement after two months of therapy, we need to use a different medication or increase the dose. It is the only FDA approved drug to use against pituitary dependent Cushing's Disease.

- Lysodren (mitotane or o,p-DDD) is a drug which attacks the part of the adrenal gland that produces cortisol. The drug is quite effective in all cases of pituitary dependent Cushing's, and has some effect in some dogs with adrenal tumors as well. The drug causes symptoms to stop within ten days on average. We start out on a twice-daily dose to stop the symptoms, which is called the induction phase. Then we move to a maintenance phase, in which the drug is given weekly. The Lysodren is a convenient way to treat Cushing's Disease. The medication can cause vomiting and diarrhea due to stomach upset. The drug does require more testing than L-deprenyl. The downsides to the drug are the testing costs, and the risk of destroying too much of the adrenal gland. When this happens it is usually temporary but can be permanent. When this occurs, too little cortisol is produced and they get what we call Addison's Disease. The symptoms of this are very sudden in onset and include lethargy, anorexia, vomiting, diarrhea, and shock. It is treatable with hormonal supplementation. When we start treatment with Lysodren, we always send home a steroid called Prednisone that is used if these symptoms start to occur and we see the pet the next day for testing. We monitor the symptoms closely and like to talk to pet owner's daily during the induction phase. When symptoms start to abate, or nine days have elapsed (whichever comes first), we perform the ACTH stimulation test. If it is normal, we go into the maintenance phase. If the levels are still too high, we re-test in a few days. If too low, we stop the medication and re-check in a few days to a week. Although not a FDA approved means of treating Cushing's Disease, veterinarians have been using this approach for many years.

- Ketoconazole is an antifungal drug that has the side effect of suppressing adrenal gland function. It is given twice daily. It can cause vomiting and diarrhea but it does not

Dr. Richard E. Dahlem :
drdahlem@orangevillavet.com
Dr. Jeffrey Horn :
drhorn@orangevillavet.com

cause Addison's Disease. Like L-Deprenyl, many dogs' symptoms do not reverse with this medication. It also is not a FDA approved means of treatment. We do not often use this treatment.

- Radiation therapy is reserved for dogs with a pituitary tumor so large it causes other neurologic side effects. If we felt this was the case, we would refer your pet to a specialist.

I hope that this helps those of you, which have pets that have Cushing's Disease. I also hope that it helps pet owners to identify the early warning signs. Cushing's Disease is a treatable disease. There is no reason why the symptoms of this disease of older pets need to decrease the quality of their lives.