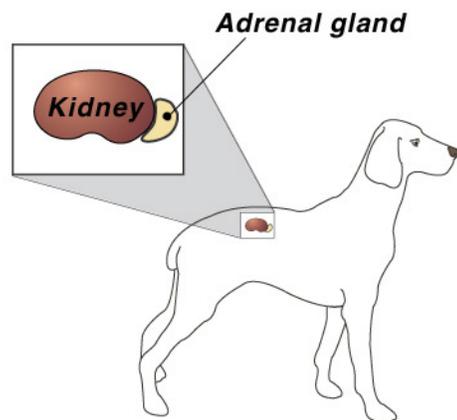


Canine Hyperadrenocorticism

Cushing's disease, Cushing's syndrome
Hyperadrenocorticism

Affected Animals: Although dogs of almost every age have been reported to have Cushing's disease, it is most common in middle-aged and older dogs. Most dogs diagnosed with Cushing's disease are at least nine to 10 years old. Slightly more female dogs are affected than male dogs. Several breeds are more commonly diagnosed with PDH than others, including poodles, terriers, German shepherds, dachshunds, beagles, and boxers. Many of these same breeds are also reported to have adrenal gland tumors at a greater frequency.

Overview: The adrenal glands are small, bean shaped organs that live in front of the kidneys. They produce several vital substances, which regulate a variety of body functions and are necessary to sustain life. The most widely known of these substances is *cortisol*, commonly known as cortisone. 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.



Cushing's disease results from excessive production of cortisol or other adrenal hormones. The medical term for this is called "hyperadrenocorticism." This excessive cortisol production can result from abnormalities in the pituitary gland of the brain that sends signals to the adrenal gland to make too much cortisol. It can also be caused by tumors within the adrenal glands themselves, or by a combination of these factors. Cortisol is a hormone that is necessary for many normal body functions.

Efforts to distinguish which form of the disease is present are important, as this can influence treatment recommendations. Blood tests and imaging procedures, including abdominal ultrasound, may be needed to make this distinction. Pituitary-dependent Cushing's disease is usually treated with medication. Adrenal gland tumors can be addressed surgically in some cases, although they can also be treated medically in situations in which surgery is not advised.

Complications due to Cushing's disease and its treatment are common, but with careful diagnosis and management, many dogs with Cushing's disease can survive for as long as two to three years or more, depending on a number of factors.

Symptoms: A variety of symptoms can result from excess cortisol, the most common of which include increased thirst and urination, increased appetite, weight gain, panting, and skin changes such as hair loss and thinning of the skin. The skin can also become abnormally dark (called hyperpigmentation), develop inflamed plaques due to calcification (called calcinosis cutis), suffer from frequent infection (called pyoderma), become greasy and foul smelling (called seborrhea), or bruise easily. Many dogs with Cushing's disease have a pot bellied appearance, muscle weakness, testicular atrophy, failure to cycle, stiff muscles (myotonia), or drooping of one side of the face due to nerve paralysis. The pot-bellied appearance of the abdomen is due to an

increase of fat within the abdominal organs, stretching of the abdominal wall as the organs get heavier, weakening of the muscles of the abdominal wall, and bloating after meals due to slow gut movement. Some dogs with Cushing's disease will even present with a rear limb lameness, as weakening of the ligaments in one or both knees can result in rupture of the crania cruciate or other ligaments.

Cause: Although the exact mechanism that causes Cushing's disease to develop is not completely understood, there are many possible causes. In general, there are two forms—pituitary dependent hyperadrenocorticism (PDH) and adrenal gland tumors (ADH). Approximately 80-85% of dogs with Cushing's disease have PDH, and about 15-20% have ADH. In very rare circumstances, both PDH and an adrenal tumor can be present in the same dog.

Most dogs with PDH have microscopic tumors that cause the excessive cortisol production, while others have larger tumors (called macroadenomas) that cause the same result. While pituitary macroadenomas are benign, they can cause potentially life threatening neurologic problems such as seizures, blindness, weakness, failure to eat and drink, etc. Most pituitary tumors causing PDH are benign.

Dogs with the less common form of the disease, adrenal gland tumors, may have either benign or malignant tumors that produce excessive amounts of cortisol from one or both adrenal glands. About half of ADH cases are caused by benign tumors, and the other half by malignant tumors.

Diagnosis: A definitive diagnosis of Cushing's disease can be difficult to obtain. When animals present with the classic signs of the disease, the diagnosis is initially suspected on the basis of those signs and the results of routine laboratory tests. As with many illnesses, a complete blood count, biochemistry profile, and urinalysis are very important tools in the initial evaluation of a dog suspected of having Cushing's disease. Usually there will be changes on these tests that may indicate the possibility of Cushing's disease. Routine imaging procedures, such as abdominal x-rays, may show changes including generalized liver enlargement, and, less commonly, adrenal gland enlargement or mineralization. Abdominal ultrasound is also used frequently in the evaluation of Cushing's suspects to evaluate the liver size and texture, the size and shape of the adrenal glands, and to look for evidence of other abnormalities that might be contributing to the dog's signs.

A more definitive diagnosis depends on the results of tests that look more specifically at adrenal gland function. The urine cortisol-to-creatinine ratio is used in some cases, but it is not a very specific test because dogs with almost any illness can have an abnormal result. This urine test is very reliable at identifying dogs who *do not* have Cushing's disease. The two most commonly used screening tests are the ACTH stimulation test, and the low-dose dexamethasone suppression test. Yet, it can be very difficult to know for sure that an individual dog has Cushing's disease, since the results of the tests can be difficult to interpret. In some cases of Cushing's Disease where hormones other than cortisol are causing the problem (called Atypical Cushing's Disease), a special ACTH stimulation test sent to the University of Tennessee must be done.

Once a tentative diagnosis of Cushing's disease is established, an attempt to distinguish which form of the disease is present should be made. The tests most commonly used to distinguish the pituitary-dependent form from an adrenal tumor are the high-dose dexamethasone suppression test, the endogenous ACTH level, and abdominal ultrasound. CAT scans can also be used to evaluate adrenal gland structure, and MRI scans can be used to look for pathology in the pituitary gland.

Treatment: There are both surgical and medical treatments for Cushing's disease. The goals with treatment are to eliminate or minimize signs due to excessive cortisol production, and to prevent potentially life-threatening complications from the disease.

The drug used most commonly to treat pituitary-dependent Cushing's disease is Trilostane. In the past, we used o,p'-DDD, also known as Lysodren or mitotane to treat Cushing's disease. However, Trilostane has fewer side effects, so Lysodren is now reserved for cases that do not respond to Trilostane. Another drug used for medical treatment of a very small set of dogs with PDH is Anipryl, or L-deprenyl. This drug is also used to treat older pets with a behavioral disorder called cognitive dysfunction syndrome. Although surgery to remove the pituitary gland has been performed, the results with medical treatment are better, and the risk of these surgeries, at least at this time, makes them difficult to recommend.

In dogs with PDH that have large pituitary gland tumors—particularly those dogs with neurological signs due to the physical presence of a large pituitary mass—the primary treatment is radiation therapy to control the growth of the tumor.

Dogs with adrenal tumors can be treated surgically or medically. The surgery is technically a very difficult one, with many potential complications during and after the procedure – 25-30% do not survive 2 weeks after surgery. A surgeon experienced in removing adrenal gland tumors should perform it. After surgery, animals often need to be supplemented with both glucocorticoids and mineralocorticoids, the two primary types of steroids normally produced by the adrenal gland. Sometimes supplementation can be tapered as the remaining adrenal gland begins to function again, but some dogs will require supplementation for life. Dogs with large and likely inoperable tumors on x-rays or ultrasound, dogs that are very sick, old, or debilitated, and dogs with suspected spread of a malignant adrenal gland tumor are all candidates for medical treatment.

Prognosis: Although most dogs with Cushing's disease are not in critical condition at the time of diagnosis, serious complications of Cushing's disease are possible. These include: high blood pressure; urinary tract infection and bladder/kidney stone formation; protein loss from the kidneys; congestive heart failure; pancreatitis; diabetes; chronic breathing problems; and blood clot formation, especially in the vessels supplying the lungs.

The outlook for surgical treatment of adrenal gland tumors is fairly good, provided that the animal survives the surgery and the period immediately after it. As a rule, dogs with benign adrenal gland tumors live longer than dogs with malignant tumors. Metastasis, or spread of a malignant tumor, makes for a worse prognosis. Such animals can be treated successfully with medication to help keep symptoms under control after surgery. Dogs that survive surgery are reported to have an average survival time of as long as 3 yrs.

Dogs treated successfully for PDH live approximately 2-3 years. Some dogs do not do that well, while others may live for 10 years or more depending on their age at the time of diagnosis, the presence of additional disorders, and the development of complications related to the treatment. Relapses are common in patients treated medically, with many dogs requiring medication adjustments due to recurrence of signs in the first year. Almost half of all dogs with Cushing's disease that die do so because of problems related either to the disease itself or its treatment. However, despite a guarded long-term prognosis, the majority of dogs can lead lives of an excellent quality with careful monitoring and attention to detail.

Prevention: The exact cause of Cushing's disease is not known, and there is no way of preventing the disease from developing. Since similar signs can occur in dogs that are treated for long periods of time with high doses of cortisone, this treatment should be avoided wherever possible. In these dogs with so-called "iatrogenic Cushing's disease," the signs should resolve as the cortisone dose is tapered. Commonly prescribed cortisone derivatives include: triamcinolone (Vetalog®, Kenalog®), dexamethasone (Azium®, Decadron®), prednisone, prednisolone, methylprednisolone acetate (Depomedrol®), betamethasone, Meticorten®, SoluDeltaCortef®, Medrol®, SoluMedrol® and others. Used appropriately, these drugs can be safe and effective. But used too much or too often, they can cause problems. Don't forget that eye, ear and topical

skin medications can contain these cortisones which can cause Cushing's syndrome if used excessively.

References:

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