

Cushing's Disease

Cushing's disease (also called hyperadrenocorticism) is an endocrine disease that is common in older dogs. Cushing's disease is rare in cats.

Cause

Cushing's disease is most commonly caused by an overactive pituitary gland in the brain. The pituitary gland is the "master gland" in the body, controlling most hormonal function. In patients with Cushing's disease, the pituitary gland over secretes a hormone that stimulates the adrenal gland. The adrenal gland then overproduces cortisol, the hormone responsible for the clinical signs of Cushing's disease. Roughly 85% of patients with Cushing's disease have the pituitary-dependent disease.

In roughly 15% of patients, an adrenal tumor is the cause of Cushing's disease. In this case, the adrenal gland over-secretes cortisol independent of pituitary influence. The tumor can be benign, but it is more commonly malignant. Although Cushing's disease is uncommon in cats, most cats with Cushing's disease have an adrenal tumor rather than a pituitary issue.

Clinical Signs

Clinical signs of Cushing's disease can vary widely from dog to dog. Most commonly, an increase in thirst and urination are seen. Some dogs break housetraining after years without an accident. Many dogs have an increase in appetite as well, and some gain weight.

Because cortisol causes muscle weakness and muscle breakdown, your dog may appear chubby around the belly, but thin in the limbs. Some dogs appear thin all over as though their muscle is wasting away. Very often, hair loss is seen, especially over the back and tail.

Cortisol has an impact on sugar metabolism in the body, so if your dog is a diabetic, their sugar will become unpredictable and difficult to control if he develops Cushing's disease. Some pets will actually develop diabetes, temporarily or permanently, at the same time, Cushing's disease is diagnosed.

Cushing's disease can also cause reversible changes in the liver. Oftentimes Cushing's is suspected when routine blood tests show liver enzyme elevations. Urine tests may be abnormal, with the urine being more dilute than normal. Cushing's can cause the kidneys to leak protein into the urine as well.

Untreated Cushing's disease can lead to some potentially life-threatening conditions. Patients can become seriously ill due to diabetes because of the effect of cortisol on insulin function. The kidneys can become stressed by the excess cortisol, resulting in blood pressure abnormalities and significant protein loss. Additionally, Cushing's increases the chance of a blood clot forming inappropriately and blocking a major blood vessel. Thankfully, these life-threatening complications are not common; they are seen more in patients with longstanding, untreated Cushing's disease.

Cats with Cushing's disease was most commonly present for profound thirst, hyperglycemia, and thin skin that tears easily.

Diagnosis

Routine screening such as a complete blood count (CBC), chemistry profile, and urinalysis are often done when Cushing's disease is suspected. These are done to assess the changes that may have occurred secondary to Cushing's disease, as well as to assess the overall health of the patient.

There are several blood tests that can help to diagnose Cushing's disease. Because Cushing's disease is a hormonal disease, and hormones fluctuate due to stress and other illnesses, there is no single test that is 100% accurate. As such, sometimes it takes 2-3 tests to confirm a diagnosis of Cushing's. One negative blood test does not rule out the possibility of Cushing's disease. It can be frustrating to have to repeat the expensive tests to confirm the disease.

An ACTH stimulation test is a 1-2 hour test to measure the cortisol before and after a stimulant is given. Dogs with Cushing's disease will have an exaggerated response to the stimulant. An ACTH stimulation test is also used to evaluate response to therapy, once started.

A Dexamethasone suppression test is an 8-hour test to measure the cortisol response to a hormone suppressing medication. Dexamethasone is a synthetic form of cortisol and when given to a normal dog, that cortisol levels will drop. In a dog with Cushing's disease, the level may drop initially, but it will rebound more rapidly than expected.

A urine cortisol to creatinine ratio is a measure of the amount of cortisol secreted into the urine. A dog with Cushing's disease will release excess cortisol in the urine. This is used as a screening tool but is not a definitive test for Cushing's. Most dogs will need a follow-up blood test if the urine cortisol to creatinine ratio supports the suspicion of Cushing's disease.

An abdominal ultrasound is often done to assess the size and shape of the adrenal glands, especially if an adrenal tumor is suspected. It is also a good test to evaluate the liver and other organs that may have been affected by Cushing's disease.

Treatment

For decades, the mainstay of Cushing's treatment has been a medication called Lysodren/mitotane. Lysodren acts directly on the over-grown cells of the adrenal gland, causing them to die off. The adrenal gland of patients with Cushing's disease are larger than normal, and Lysodren is directly toxic to these cells. The goal of the therapy is to render the adrenal gland incapable of over-producing cortisol, without dropping it too low. Most dogs will go on a daily loading dose of Lysodren for 7-10 days and then come in for recheck blood tests. Depending on the results of these tests, an additional period of loading may be necessary, or the dog might go onto twice-weekly maintenance therapy with Lysodren.

Because Lysodren acts quickly to lower the amount of cortisol in the body, some dogs feel sick towards the end of the loading period. It is important to closely monitor dogs at home while they are undergoing Lysodren loading. If lethargy, poor appetite, vomiting or diarrhea is noticed, see your veterinarian right away. Your dog might need to get a shot of prednisone or dexamethasone to bring cortisol levels up. In rare instances, hospitalization for fluids may be necessary. Lysodren therapy is considered very safe if handled by an experienced veterinarian.

Nystatin (ketoconazole) is an oral antifungal medication that suppresses the adrenal gland and is rarely used to treat Cushing's disease. It is less effective than other medications for control of Cushing's disease but is preferred by some doctors because it very slowly lowers the cortisol, rather than dropping it quickly the way Lysodren does.

Anipryl (l-depranyl) has also been used to treat Cushing's disease. Like Ketoconazole, it causes a slow drop in cortisol levels and is sometimes used in cases when close monitoring is not possible. In general, both nystatin and anipryl cause less predictable and less effective control of Cushing's disease, so they are rarely recommended.

Trilostane is a newer medication for Cushing's disease. It is currently the only FDA approved drug for the treatment of Cushing's disease. As such, it is often the first drug chosen by veterinarians. Studies show that it is safe and efficacious for the treatment of Cushing's. This means that side effects are rare and that the serum cortisol levels drop as desired on blood tests. As this drug has become more commonly used, specialists see increasing numbers of patients with ongoing clinical signs of Cushing's disease, in spite of blood tests that show adequate control of cortisol. As such, some specialists offer using the non-FDA approved drug Lysodren preferably over trilostane. The choice of drug is often multifactorial and ultimately it is up to the patient's family to make the informed decision on drug choice. Because Trilostane acts to block the production of all adrenal hormones, this medication must be handled safely by patient family members.

In the case of Cushing's disease caused by an adrenal tumor, surgery to remove the tumor may be necessary. Some of these tumors are malignant and follow-up therapy might be necessary.

Prognosis

The prognosis for most dogs with Cushing's disease is excellent, particularly those patients that are diagnosed prior to the onset of complications such as insulin resistance and kidney issues. Most patients can be adequately managed for years by an experienced doctor and routine follow up. With close monitoring and adjustments to medications, the impact of Cushing's disease on lifespan will be minimal.

Long Term Follow-Up

Cushing's disease under therapy must be monitored regularly. If Lysodren is used, during the loading phase, the patient is checked every one to two weeks. Once the patient starts maintenance therapy twice weekly, they must return for an ACTH stimulation test as often as monthly for the first 3-4 months. If they are doing well, they will be followed every 6 months or so to recheck their hormone status. It is important to remember to monitor Cushing's therapy regularly, as hormones tend to fluctuate with time.

Patients taking Trilostane are on a similar schedule for blood test monitoring.