

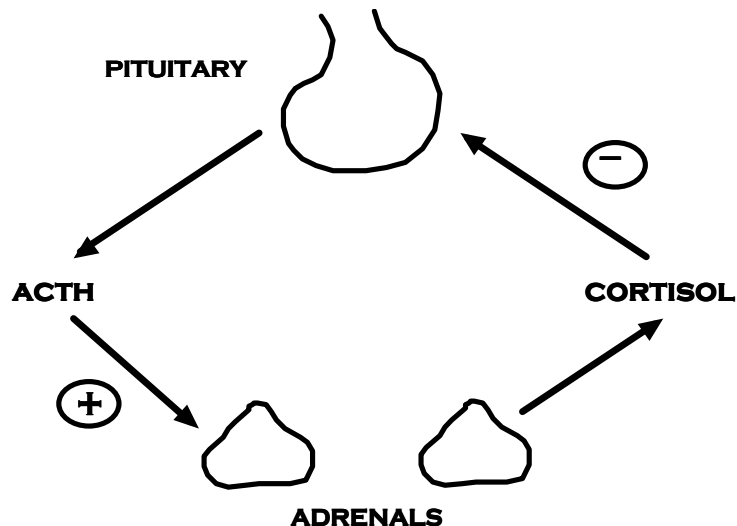
Causes and Diagnosis of Cushings Disease in Dogs

Cushings disease or hyperadrenocorticism is a common endocrine (glandular) disease in dogs. Cushings disease results from excess production of a hormone called cortisol by the adrenal glands. This handout will cover adrenal function in normal dogs and causes, clinical signs, and diagnosis of Cushings disease.

Normal Adrenal Function

Cushings disease results from overproduction of a hormone called **cortisol** by the adrenal gland. The clinical signs noted are directly caused by excess cortisol. Indeed, normal dogs receiving steroid medications can develop the exact same clinical signs noted in dogs affected with Cushings disease.

Cortisol production by the adrenal glands in normal dogs is controlled by the pituitary gland. The pituitary gland is located at the base of the brain and is also called the *master gland*. The pituitary gland produces ACTH which stimulates the adrenal glands to produce cortisol. Cortisol levels in the blood are detected by the pituitary gland. When blood levels are adequate, the pituitary gland decreases ACTH release and adrenal cortisol production decreases. This process serves to prevent insure that there are adequate, but not excess cortisol levels in the blood. This system is analogous to a home heating system where the thermostat (analogous to the pituitary) senses air temperature (analogous to cortisol level) to control the furnace (analogous to adrenal glands) to insure adequate but not excessive heating. Control of the adrenal glands in normal dogs is summarized below:

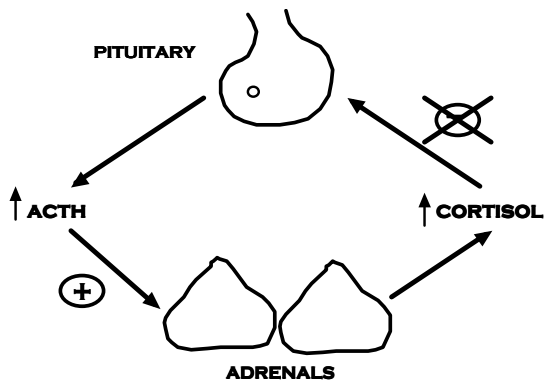


Causes of Cushings Disease in Dogs

There are two causes of Cushings disease in dogs, Pituitary Dependent Hyperadrenocorticism and Adrenal Tumor Hyperadrenocorticism.

Pituitary Dependent Hyperadrenocorticism

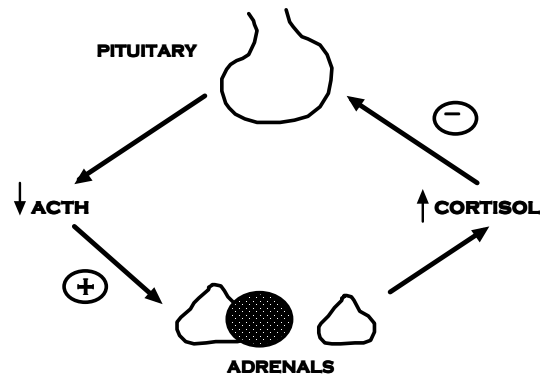
In about 90% of cases, excess production of ACTH by the adrenal gland causes elevated cortisol production by the adrenal glands to cause clinical signs. This type of Cushing's disease is called Pituitary Dependent Hyperadrenocorticism. Pituitary Dependent Hyperadrenocorticism is usually caused by a small (even microscopic) pituitary tumor which produces ACTH despite blood cortisol levels. Rarely, large pituitary tumors are found. Using the home heating analogy, elevated room temperature (analogous to excess cortisol levels) arise because of a problem with the thermostat (analogous to pituitary gland). Excess cortisol levels then cause the clinical signs noted in Cushing's disease. Both adrenal glands tend to enlarge in Pituitary Dependent Hyperadrenocorticism. Pituitary Dependent Hyperadrenocorticism is summarized below:



Adrenal Tumors

In about 10% of cases, an adrenal tumor produces excess cortisol independent of ACTH levels. These adrenal tumors are benign in about one-half of cases but malignant in the other half of cases. The pituitary senses high cortisol levels and decreases ACTH release. The remaining normal adrenal

gland decreases its production of cortisol and overtime, may decrease in size. Again, the elevated blood levels of cortisol cause the clinical signs associated with Cushing's disease. This type of Cushing's disease is called Adrenal Tumor Hyperadrenocorticism and is summarized below:



Clinical Signs of Cushing's Disease

The most commonly seen clinical signs in dogs affected with Cushing's disease, or hyperadrenocorticism, are increased water consumption, increased urinations, increased appetite, distended abdomen, hair loss, and lethargy. Signs which are also noted are susceptibility to infections and slow wound healing.

Cushing's disease usually compromises quality of life for affected dogs but is very rarely life-threatening. Fortunately trilostane treatment is generally very effective and safe method to control clinical signs and restore quality of life. Occasionally, Cushing's disease may cause no clinical signs. Since treatment of Cushing's disease has not been shown to extend lifespan, treatment of asymptomatic dogs is not recommended.

Diagnosis of Cushings Disease

Both laboratory testing and imaging studies are helpful in making the diagnosis of Cushings disease.

Laboratory Testing

Lab tests are used to both determine both if Cushings disease is present and differentiate between Pituitary Dependent Hyperadrenocorticism and Adrenal Tumor Hyperadrenocorticism.

Tests which determine whether or not Cushings disease is present are called screening tests. Screening test used in dogs include ACTH stimulation, low dose dexamethasone suppression, and urine cortisol to creatinine ratio. Screening tests should not be performed when other illnesses are present because invalid false positive results are common. False positive results can also be seen when screening tests are performed on poorly controlled diabetic dogs. The steroid medications prednisone and prednisolone will erroneously be measured as cortisol to invalidate screen test results. Screening tests should not be performed if prednisone or prednisolone has been given within the last 24 hours.

To perform ACTH stimulation, blood samples are taken before and one hour following injection of ACTH. Cortisol levels are measured in both blood samples. Dogs with Cushings disease (both Pituitary Dependent Hyperadrenocorticism and Adrenal Tumor Hyperadrenocorticism) show an exaggerated response. In about 90% of cases, ACTH stimulation identifies Cushings disease but 10% of affected dogs will have normal results. ACTH stimulation does not distinguish between Pituitary Dependent Hyperadrenocorticism and Adrenal Tumor Hyperadrenocorticism.

To perform low dose dexamethasone suppression, blood samples are taken before, 4 hours, and 8 hours following dexamethasone injection. Dexamethasone is a steroid medication which is not erroneously measured as cortisol. Dexamethasone is however, detected by the pituitary and acts to decrease ACTH release and suppress blood cortisol levels in normal dogs. Dogs with Cushings disease both types of Cushings disease fail to show suppressed cortisol levels at 8 hours. Most dogs with Pituitary Dependent Hyperadrenocorticism suppress at 4 hours but not at 8 hours while most dogs with Adrenal Tumor Hyperadrenocorticism fail to suppress at both 4 and 8 hours. This difference can be used to distinguish Pituitary Dependent Hyperadrenocorticism for Adrenal Tumor Hyperadrenocorticism.

To perform a urine cortisol to creatinine ratio, urine is collected at home and submitted for testing. Creatinine levels increase with more concentrated urine. By expressing the results as the ratio of cortisol to creatinine, differences in urine concentration are accounted for. Dogs with both types of Cushings disease can show elevated ratios.

Unfortunately, many normal dogs will have elevated urine cortisol creatinine ratios. All elevated results should be confirmed with either an ACTH stimulation or low dose dexamethasone suppression test. A normal cortisol creatinine ratio is helpful in assuring that Cushings disease is not present.

In most cases it is helpful to distinguish between Pituitary Dependent Hyperadrenocorticism and Adrenal Tumor Hyperadrenocorticism. As discussed

previously, low dose dexamethasone suppression can be useful in making this distinction. Measuring ACTH blood levels is also very helpful in distinguishing between the two causes of Cushing's disease. Dogs affected with Pituitary Dependent Hyperadrenocorticism will have elevated blood ACTH levels while those affected with Adrenal Tumor Hyperadrenocorticism will have normal to low blood levels.

Imaging Studies

Abdominal ultrasound is very helpful in distinguishing between Pituitary Dependent Hyperadrenocorticism and Adrenal Tumor Hyperadrenocorticism. In Pituitary Dependent Hyperadrenocorticism both adrenal glands are usually enlarged but normal in shape. With Adrenal Tumor Hyperadrenocorticism, one adrenal gland is usually enlarged (sometimes dramatically) and abnormal in shape while the other adrenal gland is smaller than normal.

Magnetic Resonance Imaging (MRI) and Computerized Tomography (CTI) can also be used to image adrenal glands.

