Canine Cushing's Disease (hyperadrenocorticism)

What is Cushing's disease?

Human beings, dogs, cats, and most other species of animals naturally have cortisone in their blood and in every tissue of their bodies. The cortisone is produced by a small pair of glands called the adrenal glands, one located near each kidney. In appropriate quantities, cortisone is necessary for health. If an individual does not have enough cortisone, they usually become ill and can die quickly if the condition is not treated. This is called Addison's disease. When there is too much cortisone in the system this causes illness as well, although not sudden death. This is called Cushing's disease, named for the doctor who first recognized it.

What causes too much cortisone in the system?

There are two ways that excess cortisone can happen. Medications containing cortisone are used on a daily basis for a variety of conditions and can cause signs of Cushing's disease even when used appropriately. Medications that can cause this include the following:

- Prednisone
- Prednisolone
- Methylprednisone
- Triamcinolone
- Dexamethasone

These medications can be given by injection, pill, topical skin cream, and eye and ear medications. If your pet develops Cushing's disease due to these medications it is treated by simply discontinuing your pets exposure to these medications.

When Cushing's disease occurs naturally the symptoms and internal changes can be identical to those caused by cortisol-containing medications. Cushing's disease is relatively common in older dogs but rare in cats. Fifteen percent of the time it is caused by a tumor on one of their adrenal glands which produces too much cortisol. The rest of the time it is caused by a small tumor located in the pituitary gland, a small organ located at the bottom of the brain. These tumors produce too much of a hormone called ACTH which sends a message to the adrenal glands to make more coritsol hormomes. The tumor is not "turned off" by the normal system of checks and balances that keeps the body from producing too much cortisol. The adrenal glands will get bigger in response to the constant ACTH stimulus and continue to produce cortisol, resulting in Cushing's disease. The tumors that start all this are usually benign (i.e. not cancerous tumors)

What are the symptoms of Cushing's disease?

There are several symptoms associated with Cushing's disease and not all dogs will have all the symptoms. The most common observations include the following:

1. Profound increase in thirst and urine volume. Many of these dogs urinate for a longer period of time or more frequently. Some will actually leak when they sleep. Many previously well housebroken pets will suddenly have problems urinating in the house. They will usually have increased thirst in concert with increase urination.
2. Loss of hair with no regrowth, whether hair is shaven or falls out on its own. Hair loss is most commonly observed along the back, tail, and back of rear legs. Hair loss can appear as thinning hair or as bald patches.
3. Development of muscle weakness. Owners may notice trouble climbing stairs or difficulty jumping onto furniture or into a car. Dogs may lose the ability to go on long walks or have difficulty rising after lying down. They may also appear "pot-bellied" due to abdominal muscle weakness.
4. They usually eat well and may have a ravenous appetite. They very rarely have problems with vomiting or diarrhea. They will often pant excessively.

What tests are needed?

In addition to the abnormalities observed by the owner, on physical exam the veterinarian may pick up thin skin, skin infections, muscle atrophy, and enlarged liver on abdominal palpation.

Routine blood and urine testing often reveals certain abnormalities, but again not all patients will have all these changes. Urine is often very dilute due to excessive water drinking and urinary tract infections are common. Abnormal liver enzymes are common, especially if the patient has an enlarged liver. Despite the abnormal liver test results, these patients do not have a liver problem and will not become sick or die because of the liver unless there is something else going on.

Radiographs (X-ray) and ultrasound of the abdomen are recommended to screen for other problems that could be causing an enlarged liver (like infection or cancer). Sometimes we can also pick up adrenal tumors on radiographs and ultrasound.

Once these general tests have been performed, assuming the veterinarian still thinks Cushing's disease is a possibility; specific hormone testing will need to be performed to confirm this. Tests used include the ACTH stimulation test, the urine cortisol creatinine test, and the low dose dexamethasone suppression test. Each of these tests is common and relatively effective and each has advantages and disadvantages. Additional tests may be recommended to differentiate the forms caused by the pituitary and the adrenal tumors.

What treatment is needed?

Two commonly asked questions are "Do I really need to treat my dog?" and "What happens if I don't treat my dog?" Only the owner can decide the first question. Untreated dogs tend to be weak, abnormally addicted to food and water, and generally not happy, playful, or active. If you do not see any abnormalities in your dog and believe your pet is well, then treatment is not needed. Dogs with true Cushing's disease that is untreated are not seen as being healthy by their owner. Treated dogs can live a normal quality *and* quantity of life.

Cushing's disease can be treated by surgery or lifelong oral medications. Surgery is performed to remove the tumor causing the problem and should be performed by a board-certified veterinary surgeon. Oral medication is used most often. One medication has been traditionally used to treat Cushing's disease called **mitotane** (also called Lysodren). This medication physically destroys the cells that are secreting the cortisol and is quite effective at eliminating the signs of Cushing's disease. Common side effects include lethargy, weakness, loss of appetite, vomiting, and diarrhea. The most problematic possible side effect is when mitotane destroys enough cells to cause a deficiency of cortisol and other important steroid hormones, which leads to a syndrome that is the opposite of Cushing's disease called Addison's disease. The signs of Addison's disease are very vague and include listlessness and sometimes vomiting and diarrhea. Addison's disease is treated by different (also lifelong) medications or it leads to circulatory collapse. **Trilostane** is a newer oral medication for Cushing's disease and it is the medication of choice used by our clinic. It works by inhibiting the enzyme that allows the production of cortisol hormones. It can also cause an Addison's syndrome, but it is reversible by simply discontinuing the drug. Up to 60% of patients on trilostane will experience side effects which include vomiting, loss of appetite, diarrhea, and lethargy. It helps to give the medication with food, but if you see these signs please stop the medication and call our clinic as we may try a lower dose.

Monitoring is required to make sure the medication is working properly and that your dog is on the correct dose. A test called the ACTH stimulation test needs to be performed 10-14 days after starting the medication or after each dose change, and every 3-6 months after that.