

Classifying Cushing's Syndrome: Pituitary vs Adrenal

ADRENAL OR PITUITARY CUSHINGS? WHY DO WE CARE?

Once a pet has been confirmed as having Cushing's syndrome, the next step is to determine which form of Cushing's syndrome the pet has since treatment is different for each form.

- If an adrenal tumor is present, there is a 50% chance that it is a malignant tumor. Surgical exploration is sometimes warranted so that the tumor may be removed.
- Adrenal tumors can be treated with medications just as pituitary tumors can be but the protocols are somewhat different so it is important that classification be complete.

SO WHAT TESTS WILL TELL US WHAT TYPE OF CUSHING'S SYNDROME IS PRESENT?

THE URINE CORTISOL:CREATININE TEST (UCC)

This is often the first screening test run when we suspect Cushing's Disease. It is a very simple to perform, by taking one urine sample first thing in the morning. The sample can be collected at home, to eliminate stress response of coming to the clinic. There are very few false negatives, so if this test says a dog does not have Cushing's disease, then it has effectively been ruled out. However, there are many false positives, caused by stress or illness. The Kaplan study showed that 76% of dogs with non-adrenal illness had elevated UCC.

THE ACTH STIMULATION TEST

This is often the first test done, to try and determine if your pet has Cushing's Disease. The test takes only 1-2 hours, so it can usually be done on the first day that Cushing's Disease is suspected. This test will provide a diagnosis in 80-85% of dogs with Cushing's disease, but it will not tell whether the disease is caused by an overactivity in the pituitary gland of the brain (almost always benign), or by overactivity of a tumor in the adrenal gland (can be benign or malignant).

In this test, a resting blood sample is taken to test the cortisone level in the blood. Then an injection of the hormone ACTH is given, and a second sample is taken 1-2 hours later, and cortisone levels are measured again. In the normal dog, the pituitary gland in the brain makes ACTH, which travels through the blood to the adrenal glands, and stimulates the adrenal glands to make cortisone and other hormones. The normal dogs will increase cortisone levels a little bit after getting an

injection of ACTH. But most of the time, a dog with Cushing's Disease will respond with a much higher jump in cortisone levels.

LOW DOSE DEXAMETHASONE SUPPRESSION TEST

If the ACTH stimulation test does not give us the answer we need, the low dose dexamethasone test (LDD) can be done. This test can determine not only if Cushing's disease is present, but also can give clues as to whether the problem is in the pituitary gland or the adrenal gland. This test takes a full 8 hours, so it usually can not be done on the first day. There is a particular pattern on this test that indicates a pituitary problem, and if we see it, usually no further diagnostic testing is necessary, and we go on to treatment. It is also possible that this test will confirm Cushing's Disease, but won't tell us which type. A third possibility is not very likely, but there are some dogs that actually have Cushing's Disease that does not show on either this test or the ACTH stimulation test. For those dogs, further testing is necessary.

In the LDD, a resting blood sample is taken first thing in the morning, and an injection of a small amount of dexamethasone (like cortisone) is given immediately. Then more blood samples are taken at 4 (sometimes 6) and 8 hours later. Cortisone levels are measured in all samples. In the normal dog, cortisone levels will drop dramatically after getting an injection of dexamethasone. In dogs with Cushing's disease, the levels will usually either not drop at all, or drop at 4-6 hours, then pop right back up at 8 hours. ALL of adrenal tumors don't drop at all. 60-80% of pituitary tumors drop, but then pop right back up, and the rest don't drop at all.

IMAGING

Imaging such as ultrasound, MRI, CT scan, or nuclear medicine studies may be helpful in classifying Cushing's syndrome, when the above tests fail to give us the answers we need. Ultrasound is the most readily available to us—MRI and CT are not available for pets in some areas. If a Low Dose Dexamethasone Suppression test has confirmed Cushing's syndrome but not confirmed which type, imaging of the adrenal glands can provide the information needed to complete classification. Two large or normal sized adrenal glands are typically present with the presence of a pituitary tumor as both adrenal glands will be equally stimulated by ACTH production.

If one adrenal gland looks large and the other is not visible, an adrenal tumor may be suspected (remember, the non-tumorous gland will atrophy). In the event of an adrenal tumor, ultrasound is also helpful to determine the extent of tumor spread, which is crucial to deciding for or against surgical removal of the tumor. Tumors that have already spread to surrounding structures or the liver are not usually surgically removed. Occasionally, part of the tumor may be removed to help reduce clinical signs of Cushing's Disease, but this surgery can be risky.

Keep in mind that imaging results are not forever. If blood tests are consistent with an adrenal tumor, but no adrenal tumor is seen on imaging, then either there is no adrenal tumor, or it just isn't big enough to identify yet.

THE HIGH DOSE DEXAMETHASONE SUPPRESSION TEST

This test is similar to the low dose dexamethasone suppression test except that a higher dose of dexamethasone is used and the patient having the test is already known to have Cushing's disease through prior testing. In this test, a particular pattern is seen with pituitary Cushing's Disease. But if that pattern is not seen, we still don't know whether we have a pituitary problem, or an adrenal problem. 100% of adrenal tumors will not "suppress on this test. But up to 40% of pituitary tumors will not suppress, either. But if we see suppression, we know it is a pituitary tumor.

ENDOGENOUS ACTH LEVEL

This test is felt by many to be the most accurate method of classifying Cushing's syndrome but the problem is that the test is technically challenging to run, and expensive. Serum from the patient must be frozen when transported to the laboratory in Michigan and may not thaw. The hormone ACTH is very fragile and may not survive the trip to the lab. The idea with this test is that a patient with a pituitary tumor will have high very ACTH levels, as this is what the pituitary tumor is secreting. A patient with low or no measurable ACTH levels has an adrenal tumor as the pituitary is trying its best not to stimulate the already over-active adrenal tumor. This test is usually done as a last resort, just because it is so difficult and expensive.

References:

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Wendy Brooks, DVM – VeterinaryPartner.com