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Addison's Disease (Canine Hypoadrenocorticism)

Adrenal Hormones:

The adrenal gland is so named because it is located just forward of the kidney (renal means kidney). The center of the gland is called the medulla and the outer area is called the cortex. While both areas produce hormones, Addison's disease concerns the hormones produced by the cortex; these hormones are called corticosteroids.

Corticosteroids are the hormones that enable us to adapt physiologically to stress. The glucocorticoids (such as cortisol and related synthetics, prednisone and dexamethasone and numerous others) act on the mechanics of sugar, fat, and protein metabolism. They gear the metabolism towards the preparation of burning rather than storing, fuels so as to be ready for a fight or flight situation.

The mineralocorticoids (such as aldosterone and related synthetic fludrocortisone acetate) influence the electrolytes: sodium and potassium. As a general biological rule, where there's sodium or salt, there's water. When the mineralocorticoids circulate as part of the fight or flight preparation, sodium is conserved in anticipation of blood loss so that there will be extra fluid in the vascular compartment (spare blood). When sodium is conserved, potassium is lost as part of the biological balance.

This whole picture of fat mobilization, sodium conservation etc. that is part of the fight or flight preparation is far more complex than can be reviewed here but the bottom line is: 1. Corticosteroid hormones are needed to adapt to stressful situations and without these hormones, even small stresses could lead to physiologic disaster. 2. Hypoadrenocorticism (Addison's Disease) 3. In animals with Addison's disease, there is a deficiency of the corticosteroid hormones. It is unusual to discover the direct cause of this deficiency unless the patient is taking medications that disrupt adrenal balance (like ketoconazole, Lysodrenor trilostane) but, fortunately, the disease can be managed with the administration of corticosteroid hormones even if the cause of the deficiency is unknown.

Clinical Signs:

Patients are usually young (age 4-5 years) dogs but any age dog can be affected. (This disease occurs in cats but is very rare.) There is a genetic predisposition for Addison's disease in the standard poodle and bearded collie. Female dogs are affected twice as often as males. At first signs are vague - listlessness, possibly some vomiting or diarrhea. The pet just does not seem to feel right but not in an obvious way and may seem more or less normal most of the time as symptoms wax and wane with stress. Ultimately, the disease results in a phenomenon known as the Addisonian crisis. The animal collapses in shock due to his inability to adapt to the caloric and circulatory requirements in stress. Blood sugar may drop dangerously low. Potassium levels soar and disrupt the heart rhythm because there is not enough conserved sodium to exchange for potassium. Heart rate slows, arrhythmias result. The patient may not survive this episode. Approximately 30% of dogs with Addison's disease are diagnosed at the time of an



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Addisonian crisis. Approximately 90% of the adrenal cortex must be non-functional to before clinical signs are observed.

Making the Diagnosis:

Because of the numerous symptoms that can be seen with Addison's disease, Addison's disease has earned the medical nickname The Great Imitator. You would think that you could simply look for an increase in potassium and/or drop in sodium on a basic laboratory blood panel, but it turns out spot checks of electrolyte values like this are not reliable enough for a diagnosis of Addison's disease.

Veterinarians are typically presented with a young animal in shock. There is usually no history of trauma or toxic exposure so general treatment for shock is initiated. This consists of rapid administration of fluids (usually lactated ringers solution, which has little potassium and a moderate amount of sodium) plus some glucocorticoids. By coincidence, this also happens to be similar to the specific treatment for Addison's disease so that often the patient simply recovers without the veterinarian really knowing why.

The blood panel will come back showing elevations in the renal parameters (BUN and creatinine) and thus with the elevated potassium is suggestive of acute renal failure, a condition with an extremely poor prognosis. The veterinarian may become suspicious of another diagnosis as the patient will respond well to fluid administration and most renal failure patients do not respond as well.

Addison's disease may appear in more unusual ways. Inability to maintain normal sugar levels (ultimately manifesting as a seizure disorder) may be strongly suggestive of an insulin-secreting pancreatic tumor but before a major abdominal surgery is planned, it is important to test for Addison's disease. Similarly, unexpected regurgitation of undigested food due to abnormal nerve function in the esophagus (a condition called mega-esophagus) can ultimately be caused by Addison's disease.

The only definitive test for Addison's disease is the ACTH stimulation test. The patient receives a dose of ACTH, the pituitary hormone responsible for the release of corticosteroids in times of stress. A normal animal will show an elevation in cortisol in response to ACTH while an Addisonian has no corticosteroids to respond with. This lack of response is diagnostic for Addison's disease; however, a false positive may be obtained if corticosteroids have been used in the treatment of the crisis prior to the test. Of all the commonly used corticosteroids, only dexamethasone does not interfere with the assay for cortisol; if any other steroid has been used, the test will not be valid for at least a couple of days.

Treatment:

The most important aspect of treatment for hypoadrenocorticism is the replacement of the missing mineralocorticoids hormones. One way to do this is with oral fludrocortisone (Florinef®). Florinef is given usually twice a day at a dose determined by the patient's sodium and potassium blood tests. At first, these electrolytes are monitored weekly. When levels seem stable, these blood tests are repeated two to four times per year. Often with time, it will be found that the dose of Florinef needed to control the Addison's disease will increase. This increase is unfortunate as the medication is relatively expensive. Since Florinef has glucocorticoid activity as well as mineralocorticoid activity, it is usually not necessary



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to use additional medications for treatment. Using a compounding pharmacy may be helpful in managing the costs of this particular medication, especially in a larger dog.

Another way to treat this condition is with an injectable medication called DOCP (brand name Percorten-V). This treatment is given approximately every 25 days. Electrolytes are measured prior to injections at first but testing can usually eventually be tapered to once or twice a year. There is some feeling among experts that DOCP produces better regulation of electrolytes than does oral Florinef. Some dogs however, do require glucocorticoid supplementation (such as a low dose of prednisone).

What is Atypical Addison's Disease?

Approximately one dog in 42 will have a special form of Addison's disease. To understand this form, we have to add some more details about the adrenal cortex. We have already explained that the adrenal cortex makes corticosteroids: the glucocorticoids that control sugar, fat, and protein use during stress and the mineralocorticoids that control electrolytes (mainly sodium and potassium) during stress.

The adrenal cortex has three layers: the zona fasciculata, the zona reticularis, and the zona glomerulosa. The inner two layers make the glucocorticoids and the outer zona glomerulosa layer makes the mineralocorticoids.

Most dogs get Addison's disease when all three layers of the adrenal gland are destroyed and no corticosteroid hormones of any kind can be produced. With atypical Addison's disease, the problem is limited to the layers that produce the glucocorticoids. This creates a patient who cannot regulate blood sugar normally but who is not at risk for an Addisonian crisis.

Diagnosis is still done with the ACTH stimulation test.

Treatment consists of supplementing glucocorticoid hormones, such as prednisone. Often these patients ultimately progress to the more typical Addison's disease, complete with electrolyte imbalance. A similar deficiency in glucocorticoids (but not mineralocorticoids) results when a pet has been on long-term oral glucocorticoids (such as prednisone) and medication is discontinued too abruptly. Long term glucocorticoid use leaves the outer layers of the adrenal cortex with nothing to do (and no stimulation from the pituitary gland since pills or shots are providing the body with more than enough glucocorticoids. Once the medication is withdrawn, the body is back to relying on its own adrenal glands for glucocorticoids but the gland has atrophied from lack of stimulation. This creates a deficiency in glucocorticoids similar to atypical Addison's disease and is the reason why steroid hormones are typically tapered off rather than abruptly discontinued. True atypical Addison's disease can be distinguished from overuse of medication by a plasma ACTH level (high in atypical Addison's and low with medication overuse).

What is Pacific Rimism?

Dog breeds originating in the Pacific Rim, such as the Akita and Shiba inu, commonly have elevated potassium levels on blood tests. This can be confusing when a patient has symptoms that suggest



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Addison's disease. These patients will have normal ACTH Stimulation test results if they do not have Addison's disease.

Whipworm Infection?

Whipworm infection has been known to create a syndrome nearly identical to Addisonian crisis, complete with abnormal sodium and potassium values. These patients will have normal ACTH stimulation tests but because whipworms only periodically shed eggs, fecal testing may not detect whipworm infection. If there is any question about whipworm infection, treatment should be instituted.