

Addison's Disease (Hypoadrenocorticism)

Adrenal Hormones

The adrenal glands are small, paired glands in front of the kidneys. Each gland consists of an outer cortex and an inner medulla. The glands produce several substances which regulate a variety of body functions and are necessary to sustain life. The most widely known of these substances is cortisol, commonly called cortisone or steroid, produced by the outer part of the adrenal cortex. Cortisol allows us to adapt to stress, mobilizing body stores for the "fight or flight" reaction. Also produced by the cortex and equally important is aldosterone, which is a mineralocorticoid hormone. Aldosterone hormone regulates the electrolyte and water balance of the body and is involved in the excretion of potassium and retention of sodium. As a general biological rule, where there's sodium or salt, there's water.

Deficiency of these two hormones, cortisol and aldosterone, is referred to as Addison's disease, or hypoadrenocorticism. "Hypo" is the medical term for low. Without these hormones, even small stresses could lead to shock.



Hypoadrenocorticism (Addison's Disease)

In animals with Addison's disease, there is a deficiency of adrenal hormones – cortisol and/or aldosterone. It is unusual to discover the direct cause of this deficiency unless the patient is taking medications that disrupt adrenal balance (like ketoconazole, Lysodren or trilostane/Vetoryl®). The most common cause of Addison's disease is autoimmune destruction of the adrenal glands. Infection of, cancer of or trauma to the adrenal glands can also rarely cause Addison's disease. Fortunately, the disease can be managed with the administration of hormones even if the cause of the deficiency is unknown

Symptoms of Addison's Disease

Patients are usually young (age 4-5 years) female dogs. Addison's Disease does occur in cats but is very rare. Predisposed breeds include: the Great Dane, the West Highland White terrier, all sizes of poodles, Labrador retrievers and Portuguese water dogs. At first signs are very vague and can wax and wane:

- Listlessness, poor appetite
- vomiting or diarrhea (especially bloody diarrhea), abdominal pain
- weight loss
- drinking and urinating excessively
- muscle tremors, shaking, weakness, collapse

Ultimately, if undiagnosed and untreated, the disease results in a phenomenon known as the "Addisonian crisis." The animal collapses in shock due to its inability to adapt to the caloric and circulatory requirements in stress. Blood sugar and protein 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, and abnormal heartbeats result. The patient may not survive this episode, if not treated promptly. **Approximately 30% of dogs with Addison's disease are diagnosed at the time of an Addisonian crisis.** Because the animal becomes dehydrated, an Addisonian crisis can be easily mistaken for kidney failure or septic shock. Patients rapidly improve and respond with fluid therapy, but symptoms return within days to weeks.

Making The Diagnosis

Veterinarians are classically 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 intravenous fluids 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 kidney values (BUN and Creatinine) and elevated potassium, suggestive of acute kidney failure.

Addison's disease may present in more unusual ways. Because of the numerous symptoms Addison's disease can be present with, Addison's disease has earned the medical nickname "the Great Pretender."

- Low blood sugar or blood protein (albumin)
- regurgitation of undigested food due to abnormal nerve function in the esophagus (a condition called Megaesophagus)
- high white blood cell (lymphocyte) count
- high calcium

On chest x-rays, the heart will often look small due to low blood volume, and the esophagus might be enlarged. Rarely, if the esophagus is affected, the dog may have aspiration pneumonia from accidentally breathing food and water into the lungs. If potassium is high, the ECK might show typical abnormal heart rhythm that goes along with that problem.

The only definitive test for Addison's disease is a timed blood test called the ACTH stimulation test. The patient receives a dose of ACTH, the pituitary gland hormone responsible for the release of corticosteroids from the adrenal glands 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. Only dexamethasone does not interfere with the test for cortisol; if any other steroid has been used, the test will not be valid for at least a couple of days.

An ultrasound of the abdomen may be suggested if there are signs pointing to other possible diseases, or the rare case of Addison's disease caused by trauma or infection.

Treatment After The Crisis

The most important aspect of treatment for hypoadrenocorticism is the replacement of the missing mineralocorticoids hormones. Currently, there are two drugs on the market that do this:

- *Fludrocortisone (Florinef®)* – pills given by mouth, 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 2 to 4 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 is unfortunate as the medication is relatively expensive. Since Florinef® has glucocorticoid activity as well as mineralocorticoid activity, it is usually not necessary to use additional medications for treatment.
- Another way to treat this condition is with an injectable medication called *DOCP (Percorten-V®, Zycortal®)*. This treatment is given every 25-28 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).

Salting the patient's food is sometimes recommended to assist the patient with sodium balance. Once Addison's Disease is diagnosed, lifelong replacement of adrenal hormones is necessary. Some of these medications may have to be increased during periods of stress, such as when traveling, if your dog is going to be boarded, or if your dog has to undergo surgery.

What is "Atypical Addison's Disease?"

Approximately one dog in 42 will have a special form of Addison's disease. Most dogs get Addison's disease when all three layers of the adrenal gland are destroyed and no corticosteroid hormones can be produced. With atypical Addison's disease, the problem is not with the adrenal gland itself but with the pituitary gland, which is located at the base of the brain. The normal pituitary gland secretes ACTH (adrenocorticotrophic hormone), which stimulates the adrenal cortex to produce glucocorticoids. Without this hormone, these two areas of the adrenal gland atrophy but the zona glomerulosa remains normal. This yields a patient who cannot regulate blood sugar normally but who is not at as high a risk for an Addisonian crisis. Diagnosis is still by ACTH stimulation test and an endogenous ACTH level. The latter test is difficult to perform, expensive, and usually not necessary. Treatment is supplementation of glucocorticoid hormones, such as prednisone. It should be noted that often these patients progress to the more typical Addison's disease complete with electrolyte (sodium and potassium) imbalance.

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 very confusing when a patient has symptoms that suggest Addison's disease or kidney failure. These patients will have normal ACTH Stimulation test results if they do not have Addison's disease.

Whipworm Infection?

Whipworm infection (an intestinal parasite) 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.

What is the Prognosis for Dog with Addison's Disease?

Once treated and stabilized, most patients with Addison's Disease live a basically normal life, as long as they take their medications regularly, and are monitored by a veterinarian. If undiagnosed and untreated, the Addisonian crisis can be potentially fatal.

There is a newsgroup for owners of pets with Addison's disease. To subscribe visit: <http://groups.yahoo.com/group/k9Addisons/>.

References:

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