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News

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ADDISON'S DISEASE (HYPOADRENOCORTICISM)

Addison's disease, or hypoadrenocorticism, is a well-recognized syndrome caused by the inadequate production of glucocorticoids and/or mineralocorticoids from the adrenal glands.

Immune-mediated destruction of the adrenal cortices leading to **primary adrenocortical failure** is believed to be the most common cause of hypoadrenocorticism. Other causes of adrenocortical destruction include mycobacterial infection, fungal infection, treatment with o,p'-DDD, hemorrhage, and neoplasia. **Secondary hypoadrenocorticism** can occur when the hypothalamic-pituitary-adrenal axis malfunctions due to brain neoplasia or inflammation, or the adrenals atrophy from exogenous steroid administration. Secondary hypoadrenocorticism causes glucocorticoid deficiency but aldosterone levels usually remain adequate (normal electrolytes). There is also evidence that primary adrenal disease, on occasion, can cause glucocorticoid deficiency without concurrent mineralocorticoid deficiency.

Because of the often vague nature of clinical signs and inconsistent laboratory abnormalities, Addison's disease is often overlooked in the differential diagnosis.

Signalment

Most reports of dogs with Addison's disease (both typical and atypical) have noted a higher prevalence in young to middle-aged, female dogs. In one study, the majority were larger-breed dogs with body weight > 20 kg. Familial hypoadrenocorticism has been reported in several breeds including the Standard Poodle, Bearded Collie, Leonberger, Nova Scotia Duck Tolling Retriever, Portuguese Water Dog, Old English Sheepdog, Labrador Retriever, Standard Schnauzer, Soft-Coated Wheaten Terrier, Basset Hound, English Springer Spaniel, German Shorthaired Pointer,

Doberman Pinscher, Newfoundland and West Highland White Terrier. Any breed or mixed breed of dog can be affected. The condition can also occur in combination with autoimmune thyroiditis, a situation called Schmidt's syndrome in people. Addison's disease is quite rare in cats.

• Typical Clinical Presentations

Historically, dogs with Addison's disease have vague complaints such as intermittent anorexia, vomiting, diarrhea, weakness, lethargy, depression and weight loss. In the acute form of the disease, weakness and depression can progress to collapse, hypovolemic shock, and bradycardia.

• Unusual Clinical Presentations

Megaesophagus. Dogs with both typical and atypical Addison's disease have reportedly had poor esophageal contractility leading to megaesophagus. Regurgitation may be their only complaint on presentation. Some dogs present with aspiration pneumonia as a result. Thus, all dogs with megaesophagus should be evaluated for hypoadrenocorticism.

Hypoglycemia. About 16-33% of affected dogs are hypoglycemic. This can present as weakness, ataxia and disorientation, or even acute collapse with seizures.

Gastrointestinal hemorrhage. Melena and/or hematemesis have been reported in both typical and atypical Addison's cases. Gastrointestinal ulcers may form as a result of the hypovolemia due to aldosterone deficiency (poor perfusion and vascular stasis within the intestines).

Pure aldosterone deficiency. Although rarely seen, some dogs with abnormal electrolytes and normal ACTH stimulation tests have been confirmed to be aldosterone deficient. Once all other causes of hyponatremia and hyperkalemia are ruled out, aldosterone levels are

ADDISON'S DISEASE (CONT'D)

measured before and after ACTH stimulation. In some cases, this rare manifestation of Addison's disease is confirmed at necropsy.

Laboratory Findings

The hemogram may show anemia, absolute lymphocytosis and eosinophilia, but a normal hemogram and chemistry profile does not rule out hypoadrenocorticism. Dogs with Addison's disease can have low or low-normal glucose concentration, hypoalbuminemia, low serum cholesterol concentration, hypercalcemia, low sodium and high potassium concentrations from aldosterone deficiency, azotemia, and low urine specific gravity. About 10% of dogs with Addison's disease have normal serum electrolyte concentrations (so-called "atypical" Addison's disease).

Diagnosis

The test of choice for diagnosing hypoadrenocorticism is the ACTH Stimulation Test. Affected dogs have little or no rise in cortisol levels in response to exogenous ACTH. It is currently not known whether the majority of dogs with atypical Addison's disease have primary or secondary hypoadrenocorticism, or whether they will progress to develop mineralocorticoid deficiency as well. Measuring aldosterone levels in affected dogs may help clarify their type of hypoadrenocorticism, but whether this test is predictive of developing mineralocorticoid deficiency is not known. The most reliable way to distin-

guish primary from secondary disease is to measure the endogenous ACTH concentration. In primary hypoadrenocorticism, endogenous ACTH concentrations are high, whereas they are low or very low in the secondary form of this disease.

Immune-mediated adrenal disease may be accompanied by other immune disorders including hypothyroidism, diabetes mellitus, hypoparathyroidism, inflammatory bowel disease, glomerulonephritis, and chronic hepatitis. When the combination of Schmidt's syndrome is present, correcting the thyroid dysfunction can improve control of the Addison's disease.

Treatment

Regardless of the primary or secondary nature of Addison's disease, treatment requires replacement doses of prednisone (0.1-0.2 mg/kg/day) to correct their glucocorticoid deficiency. During times of stress, such as grooming, boarding, illness or surgery, extra prednisone may be necessary. For those with mineralocorticoid deficiency as well, fluid therapy is often needed to reestablish normal electrolyte balance, and mineralocorticoid replacement with daily flucortisone acetate (Fluorinet®), or injections of desoxycorticosterone pivalate (Percorten®) given every 3-4 weeks is needed. Dietary supplementation with salt is rarely necessary.

References: Lifton et al., JAVMA 209: 2076-2081, 1996; Peterson et al., JAVMA 208: 85-91, 1996; Kintzer and Peterson, J Vet Int Med 11: 43-49, 1997.

BASAL CORTISOL CONCENTRATIONS FOR ASSESSING ADRENAL FUNCTION

The only approved ACTH preparation (Cortrosyn®: Organon Pharmaceuticals, West Orange, NJ) has recently become available again, after a period of back-order. While other forms of ACTH may be available, but their potency may not have been substantiated.

If a reliable source of ACTH is unavailable, basal cortisol concentrations can be used for assessing adrenal function. While this is not the ideal adrenal function test (because of possible wide daily fluctuations), it can be clinically useful when evaluated in conjunction with the patient's clinical signs and other laboratory findings.

Diagnostic screening test for hyperadrenocorticism:

- Basal cortisol are **not** useful.
- Consider urine cortisol:creatinine ratio (UCCR) and low-dose dexamethasone suppression (LDDS) test.

Diagnostic screening test for hypoadrenocorticism:

- Basal cortisol < 1 ug/dl is consistent with hypoadrenocorticism, if clinical signs are supportive.
- Basal cortisol > 5 ug/dl excludes a diagnosis of hypoadrenocorticism
- Basal cortisol > 1 ug/dl and < 5 ug/dl is nondiagnostic.

Monitoring mitotane (Lysodren®) therapy for hyperadrenocorticism:

- If basal cortisol is < 1 ug/dl, consider stopping therapy and repeating the test in 2 to 4 weeks.
- If basal cortisol is > 1 ug/dl and < 5 ug/dl, and the patient is asymptomatic for hyperadrenocorticism, consider stopping the loading phase of mitotane therapy and starting maintenance therapy, or continuing with maintenance therapy at the same dosage of mitotane. Basal cortisol should be re-measured in 1 to 3 months.
- If basal cortisol is > 1 ug/dl and < 5 ug/dl, and the patient is symptomatic for hyperadrenocorticism, continue or start maintenance therapy and repeat the basal cortisol in 2 to 4 weeks.
- If the basal cortisol is > 5 ug/dl, consider continuing the loading phase of mitotane therapy for a longer period (usually 3 to 5 days), or raising the maintenance dosage by 25 to 50% and repeating the basal cortisol concentration immediately following the reloading period, or 1 month following maintenance therapy at the higher dosage.