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CANINE CUSHING'S DISEASE

What is Cushing's Disease?

Cushing's Disease is a disease in which the adrenal glands overproduce certain hormones. Another medical term for this disease is *hyperadrenocorticism*.

The adrenal glands are located in the abdomen, near the kidneys, and produce several vital substances which regulate a variety of body functions and are necessary to sustain life. The most widely known of these substances is cortisol, commonly known as cortisone. Either deficient production or excessive production of these substances may be life-threatening

How does this disease occur?

There are three mechanisms by which this disease can occur. Regardless of the cause, the clinical signs are essentially the same. It is important to identify the cause, however, because the various forms are treated differently and have different prognoses.

Pituitary gland tumor. The most common cause of Cushing's Disease (85% of all cases) is a tumor of the pituitary gland. The Pituitary Gland is located in the brain. The tumor may be either benign or malignant. It causes the pituitary gland to overproduce a hormone, which stimulates the adrenal glands to produce too much cortisol. The tumor may be either microscopic or quite large. Depending on the size of the tumor, the presence of signs other than Cushing's will be variable. Generally, if the activity of the adrenal gland can be controlled, many dogs with this form of Cushing's Disease can live normal lives for many years as long as they take their medication and stay under close medical supervision. Growth of the pituitary tumor would give the patient a less favorable prognosis.

Adrenal gland tumor. Cushing's Disease may be the result of a benign or malignant tumor of the adrenal gland. If benign, surgical removal cures the disease. If malignant, surgery may help for a while, but the prognosis is less favorable than for a benign tumor.

Iatrogenic. Iatrogenic Cushing's Disease means that the excess of cortisone has resulted from excessive administration of the drug cortisone. This may occur from oral or injectable medications. Although the injections or tablets were given for a legitimate medical reason, their excess is now detrimental.

What are the clinical signs?

The most common clinical signs associated with Cushing's Disease are a tremendous increase in appetite, water consumption, and urination. Lethargy, or lack of activity, and a poor hair coat with bald spots are also common. Many of these dogs develop a bloated appearance to their abdomen due to an increase of fat within the abdominal organs and a stretching of the abdominal wall as the organs get heavier. The pot-bellied appearance also develops because the muscles of the abdominal wall become weaker. Panting is another common finding with this disease. Excessive cortisol in the body can also suppress the immune system and predispose to infections.

How is it diagnosed?

Animals with Cushing's disease will often show abnormalities on routine screening tests. A marked elevation in a liver enzyme *serum alkaline phosphatase* (ALKP) is present in over 90% of cases. Mild elevations of other liver enzymes, cholesterol and glucose are often present. However none of these tests are diagnostic.

A number of special tests are necessary to diagnose and confirm Cushing's Disease. The primary ones are the ACTH Stimulation Test and the Low-Dose Dexamethasone Suppression Test. Sometimes other tests are needed to decide which form of the disease is present. Although some of these tests are somewhat expensive, they are necessary.

What are the treatment options?

Iatrogenic Cushing's Disease: Treatment of this form requires a discontinuation of the cortisone that is being given. This must be done in a very controlled manner so that other consequences do not occur. Unfortunately, this usually results in a recurrence of the disease that was being treated by the cortisone.

Adrenal Tumor. Treatment of an adrenal tumor requires major surgery. Although this surgery is risky, if it is successful and the tumor is not malignant, there is a good chance that the dog will regain normal health. If surgery is not an option, some of these can be well managed with the medication Lysodren. Lysodren™ is the primary drug used to destroy the abnormal adrenal tissue. Lysodren™ is also known as mitotane or o,p'-DDD. If not enough drug is used, the abnormal tissue persists and the disease continues. If too much is used, most or all of the adrenal cortex will be destroyed, which can be life-threatening. Lysodren does have many side-effects including anorexia, lethargy, vomiting and diarrhea. Therefore, careful monitoring of the dog is necessary in order to achieve good results. Because the pituitary is not being affected by the treatment, it continues to stimulate the adrenal gland. This means that continued treatment is necessary. Although a cure is not possible, control is possible for many years.

Pituitary Tumor: There are several options in the treatment of the pituitary-induced form of Cushing's Disease. Besides Lysodren, Trilostane, Nizoral (Ketoconazole) and Anipryl (L-Deprenyl) are also used. Like Lysodren, Nizoral can have side-effects and needs persistent monitoring. Trilostane is the newest drug available to treat Cushing's disease. Anipryl has no reported side-effects, and monitoring is not as crucial, it also is less effective than the other drugs available. All these medications have a considerable cost associated with them, and therapy is usually life-long.

INSTRUCTIONS FOR THE MEDICAL TREATMENT OF CUSHING'S DISEASE WITH LYSODREN

Treatment of this form involves an *initiating phase* and a *maintenance phase*. The *initiating phase* arrests the disease and restores the dog to a more normal state. Some of the clinical signs, especially increased food and water intake, should stop within the first 1-3 weeks. Other signs, such as a poor hair coat or a bloated abdomen, may take several weeks or months to correct. The *maintenance phase* represents the phase of long-term therapy. This phase lasts the rest of the dog's life.

You must continually monitor your dog's food and water intake. We expect both to return to a normal level. Water intake should be less than 1 oz per pound (66 cc per kilogram) of body weight per day, but don't limit the water if your dog needs to drink more. For your dog this amounts to _____ . The food amount should be measured each day. At least two feedings per day are preferred.

Initiating Phase

1. Give _____ Lysodren™ tablet(s) one time per day beginning on _____ for 9 days or until one of the following occurs:
 - a) Your dog's water intake drops to the 1 oz per pound (66 cc per kilogram) per day level or _____ per day.
 - b) Your dog's appetite returns to normal or it takes 15-30 minutes to eat when it would normally eat in much less time.
 - c) Your dog does not eat a regular meal.
 - d) Your dog vomits.
 - e) Your dog has diarrhea.
 - e) Your dog becomes unusually listless.
2. Return in nine days or when one of the above occurs for another ACTH stimulation test. This test should be done early in the morning and will require your dog to be in the hospital for about 4-5 hours. If the test is abnormal, the initiating phase will continue. If the test is normal, the maintenance phase will begin.
3. If loss of appetite, vomiting, diarrhea, or listlessness occurs, give _____ tablet(s) (_____ mg) of hydrocortisone twice daily for two days. DISCONTINUE THE LYSODREN™ TABLETS. If vomiting prevents oral administration, your dog must be seen by a veterinarian for administration of proper medication by injection. When you begin this treatment, please call us for consultation and instructions.

Following the first two days of treatment with _____ tablet(s) twice daily, give _____ tablet(s) twice daily for two more days, then _____ tablet(s) twice daily for three days, then _____ tablet(s) once every other day for one week. At the end of that time, make an appointment so we can assess the situation and give you further instructions on Lysodren administration.

4. Report any other changes in your dog's behavior that are out of the ordinary. This disease and this treatment can result in several abnormal behaviors. However, your dog can also have other diseases that occur concurrently but independently of Cushing's disease. It is important that we differentiate between the two situations so that proper treatment can be taken.
5. Stay cautiously optimistic. This is a serious disease, but many dogs with Cushing's disease enjoy a greatly improved quality of life for many years.

Maintenance Phase

When regulated, your dog will take Lysodren™ approximately once weekly. An ACTH stimulation test will be necessary about every 3-4 months to be sure that regulation is satisfactory. At the appropriate time, the specifics of the maintenance phase will be explained.

Give _____ tablet(s) every _____ days.