

## CUSHING'S DISEASE

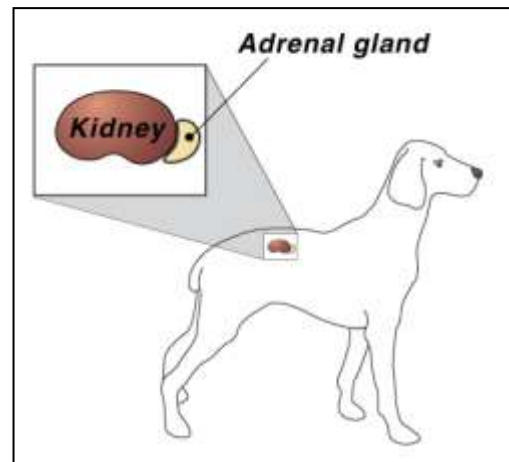
### *What is Cushing's Disease?*

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

The adrenal glands 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. Decreased 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 type of Cushing's Disease 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 tumor causes the pituitary to overproduce a hormone that stimulates the adrenal glands. Excessive cortisol secretion then occurs. The tumor may be microscopic or quite large. Depending on the size of the tumor, clinical signs other than Cushing's Disease may be present. 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.

**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 cortisol has resulted from excessive administration of a steroid. 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 an increase in appetite, water consumption, and urination. Lethargy, or lack of activity, and a poor hair coat 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.

### *How is it diagnosed?*

A number of tests are necessary to diagnose and confirm Cushing's Disease. The two most common tests to detect Cushing's Disease are the ACTH Stimulation Test and the Low-Dose Dexamethasone Suppression Test. Other tests are needed to decide which form of the disease is present. An ultrasound examination can be a valuable part of the testing process. This permits visualization of the adrenal glands and determines their size and the presence of a tumor. 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 steroid that is being given. This must be done in a very controlled manner so that other complications do not occur. Unfortunately, it usually results in a recurrence of the disease that was being treated by the steroid. Because there may have been adverse effects on the adrenal glands, treatment is also needed to correct that problem.

**Adrenal Tumor.** Treatment of an adrenal tumor requires major surgery. Although this is a high risk surgery, if 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 patients can be managed with the medication discussed next.

**Pituitary Tumor: Treatment** of the pituitary-induced form of Cushing's Disease is the most complicated. There are two drugs commonly used: Trilostane and Lysodren™. Trilostane is given once or twice daily and has little, if any, side effects but is expensive. Blood tests ( 4-6 hours after dosing) are required when using this medication usually 10, 30 and 90 days after starting treatment then every 4-6 months. Most pets with uncomplicated Cushing's Disease (no complications such as diabetes mellitus, etc.) can be treated with Trilostane and most clinical signs will resolve. If a pet does not improve after two to three months of Trilostane therapy, Lysodren™ therapy is often recommended.

Lysodren™ is the primary drug used to destroy the abnormal adrenal gland 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. 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 achieved with either treatment, control is possible for many years if the tumor is small. If the tumor is large, local effects of the tumor invading surrounding tissues in the brain can be the limiting factor in survival.

## INSTRUCTIONS FOR LYSODREN TREATMENT OF CUSHING'S DISEASE

Treatment for Cushing's Disease involves giving a drug called (Lysodren (Mitotane)) that selectively destroys part of the adrenal gland that is producing too much cortisol in your dog's body. There are 2 stages of treatment: 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.

### 1) Induction phase of treatment

Give your dog only 2/3 of its normal daily intake. Divide this into 2 equal meals as it is essential we keep them on the hungry side so any reduced appetite will be easily noticed by you. Wash hands thoroughly after handling whole mitotane tablets and preferably use gloves to handle cut tablets. Do not cut the tablets on your food preparation surfaces.

Start on Saturday \_\_\_/\_\_\_/\_\_\_ and give \_\_\_\_\_ of a mitotane tablet in the morning & \_\_\_\_\_ of a mitotane tablet at night immediately after they have eaten. This enhances drug absorption and ensures there has been no reduction in appetite before the drug is given.

### Stop giving mitotane and contact us if you notice any of the following

- any decrease in appetite eg leaving any food, pausing during the meal – if you time how long they take to normally eat a meal it helps so when they get slow you know their appetite is waning
- the volume of water drunk is less than 60ml/kg/day ie less than \_\_\_\_\_/day
- vomiting, diarrhoea, listless, depression

Ideally we want to stop treatment as soon as there is a decrease in appetite or thirst. Any of the other signs are an indication the end point of the induction phase has been reached or exceeded, the hospital should be contacted immediately and you may be told to start the **antidote** prednisolone. (If we are closed contact the after hour emergency service on \_\_\_\_\_)

A small percentage of dogs do not tolerate mitotane well and may show lethargy, vomiting, diarrhoea, weakness or inappetence in the first few days of therapy. These signs are the same as when the end point of induction has been reached, so if any these signs develop stop the treatment and we will need to evaluate whether it is a reaction to the drug or the end stage has been reached.

We need to perform a blood test 2 days after the mitotane has been stopped to see if we have adequately suppressed cortisol production. 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.

## 2) Maintenance phase of mitotane treatment

This is a life long treatment. You need to give \_\_\_\_\_ tablets a week ideally give \_\_\_\_\_ tablet morning and \_\_\_\_\_ tablet at night on \_\_\_\_\_.

*Always feed first* before giving the tablet so any reduction in appetite can be noticed before the tablet is given.

The need for the medication may vary with time hence regular rechecks and blood tests are important. (Once stabilized usually it is every 3-6 months). If you notice an increase in appetite, thirst or urination the blood test may need to be brought forward. If your dog seems unwell, inappetent, lethargic or has any vomiting or diarrhoea contact the hospital before the next dose of mitotane is given. (More likely to occur at stressful times)

Occasionally other diseases are masked by Cushings Disease and once you have treated the Cushings Disease these other diseases become apparent. Two of the most common are arthritis and flea allergy. We can treat these if they arise.

Remember: always use gloves or wash hands thoroughly after handling the tablets  
do not use your food preparation surfaces to cut the tablets  
stop the tablets as soon as there is a reduction in appetite, thirst, any depression, vomiting or diarrhoea  
the prednisolone tablets are the **antidote** if your dog becomes lethargic, weak, starts vomiting or diarrhoea. Please speak to a vet prior to starting them.

Although it is quite involved, especially initially, the results to treatment are definitely worth the effort. This is a serious disease, but many dogs with Cushing's Disease enjoy a greatly improved quality of life for many years.

## Instructions For Trilostane treatment

Starting doses :

5-20kg =60mg/d

20-40kg = 120mg/d

>40kg =240mg/d

blood test 4-6 hours after dosing at 10,30 & 90days then every 4-6 months

if post acth cortisol is < 20 nmol/l then stop rx for 48hrs and reintroduce at a lower dose

if post acth cortisol is > 120nmol/l , then increase the dose

if dose is in-between and dog is clinically well controlled then no change in the dose , but if clinically not well controlled then administer twice daily

if blood test is outside of the 4-6 hrs after trilostane then post acth should be between 20-250 nmol/l