**Hyperadrenocorticism (Cushing’s Disease)**

**Explanation of the Disease**

Hyperadrenocorticism is an excessive production of the hormone Cortisol. Cortisol is a stress hormone produced by the adrenal glands which are located near the kidneys. Cortisol is important for the body’s response to stress, metabolism of glucose and control of blood pressure. The production of cortisol is regulated and controlled in the body by the pituitary gland in the brain. The pituitary gland has the ability to detect when there is sufficient, inadequate or excess cortisol within the body and then regulates the level of cortisol by releasing its own hormone (adrenocorticotrophic hormone) which in turn stimulates the production of cortisol from the adrenal glands.

Cushing’s disease is the result of either;

Disease of the pituitary gland, most commonly a benign tumour of the pituitary gland. This occurs in approximately 85% of cases.

or

Disease of the adrenal gland which is most commonly a benign or malignant tumour of the gland.

The result of either scenario is an uncontrolled production of cortisol, and thus persistently elevated levels of this hormone present within the body.

**Clinical Symptoms**

Cushing’s disease is a relatively common disease of middle aged to older dogs and is rare in cats. It is also more common in small breed dogs. The clinical signs of Cushing’s disease are associated with the long-term effects of cortisol on the body and include:

- Increased thirst and increased urination
- Increased appetite
- Hair loss and/or changes of the skin
- Muscle loss/wastage and increased fat deposition (pot-bellied appearance)
- Increased panting
- Lethargy and weakness
- Neurological signs

**Diagnostic Procedures**

To diagnose Cushing’s disease, a combination of tests are performed. Initially a thorough physical exam by the veterinarian and history is required and then this is often followed with a blood test to
assess internal organ function and rule out other possible causes of the above clinical signs; such as diabetes, liver or kidney disease. An abdominal ultrasound can also be useful in assessing for changes within the adrenal glands and rule in or out an adrenal based tumour.

A more specific test called a ‘Low Dose Dexamethasone Suppression Test’ (LDDST) may be performed. This test helps to confirm the diagnosis but also helps differentiate between pituitary based Cushing’s and adrenal based Cushing’s.

For the LDDST we take a baseline cortisol level of your pet via a blood sample, and then we inject a small amount of dexamethasone, a synthetic glucocorticoid. We then check their cortisol levels at 4 and 8 hours post dexamethasone injection. If we see lack of suppression at 4 and 8 hours we strongly suspect your pet has hyperadrenocorticism.

**Treatment**

In cases where there is an adrenal tumour causing Cushing’s disease, surgery can be an option for treatment. Prior to surgery, imaging with X-rays, CT or MRI is often required to ensure the tumour has not spread to other areas of the body. Surgery is performed by veterinary specialists and is extensive so some owners may elect for medical management instead.

In cases where there is a pituitary based tumour causing disease, surgery is not an option and therefore medical treatment is required. Medical treatment aims to manage the production of cortisol from the adrenal glands by targeted destruction of the adrenal cortical cells which are responsible for producing cortisol. Treatment is not a cure and is required life-long. The treatment is in the form of a once or twice daily capsule which should be given with food. Monitoring after starting treatment is extremely important.

Trilostane is the preferred treatment for your pet with pituitary based Cushing’s, this medication inhibits an enzyme crucial for the production of cortisol within the body. The medication should ALWAYS be given WITH FOOD. A blood test to monitor response to medication is required 7-10 days after starting treatment and dose adjustments may be made accordingly.

**Monitoring Requirements**

Monitoring is done through a specific blood test called an ACTH stimulation test. This test aims to assess the level of cortisol being produced by the adrenal glands in light of the medication which is hopefully controlling excessive production. To perform the ACTH stimulation test your pet will require a day in hospital. During that day we take a baseline blood sample to check to the resting cortisol level of your pet, and then we inject a medication called Synacthen and take another blood sample one hour later. The result of this test will influence the dose of medication required. Medication should be administered with food as usual on the morning of the test.

The ACTH stimulation test is performed initially 10 days after starting treatment then every 2 weeks until your pet is stable on its dose. Ongoing management with the ACTH stimulation test 1 month after a stable dose is achieved and then every 3-6 months ongoing is required. In addition to the ACTH stimulation test, a thorough health check and monitoring of your pet’s electrolytes, liver and kidney function via blood tests is required every 3-6 months.
You will be required to monitor your pet’s clinical signs at home, as this can be a good indication as to how they are responding to treatment and to ensure no adverse side effects to treatment are occurring. You should notice a reduction in thirst, appetite and urination. Better weight control and general increase in energy levels after starting treatment. If lethargy, depression, weakness, inappetence, vomiting, diarrhoea, dehydration or blood in the faeces then please cease medication and bring your pet in straight away.

**Side Effects of Trilostane**

The medication can have adverse side effects in some patients, thus **careful dosing and monitoring is essential**. The side effects are usually the result of the drug causing excessive destruction of the adrenal cortical tissue and presents as signs of vomiting, lethargy, and poor appetite. Should any of these signs be noted they should be reported straight away to a veterinarian as dose adjustments or stopping therapy may be required.

Mild lethargy and appetite reduction are not uncommon especially when medication is started and the body adapts to its hormonal changes. Also vomiting and diarrhoea may be noticed. Side effects are more common if over dosing occurs and so it is important to regularly have blood tests to check the dose of medication is correct.

Addisonian reactions is when there is not enough cortisol available to the body, this may be because of an overdose or as a result of the ability of Lysodren (an older, less safer treatment drug) to destroy adrenal tissue. Although Trilostane does not destroy the adrenal cortex, idiosyncratic reactions have been reported. This means it can occur unpredictably and at any dose. In these cases, discontinuation of Trilostane often resolves the issue, otherwise supplementation with prednisolone may be required.