

# Hyperadrenocorticism (Cushing's Syndrome)

## ABOUT THE DIAGNOSIS

Hyperadrenocorticism, also called Cushing's disease or Cushing's syndrome, is a health disorder of dogs that is caused by abnormally high levels of corticosteroid (cortisone-like) hormones in the body. Corticosteroids are natural hormones produced by a pair of small glands called the adrenal glands. The adrenal glands are located inside the abdomen, beside the kidneys. The function of the adrenal glands is to make substances that are essential to life, including the corticosteroid hormones. The production of these hormones needs to be closely controlled in the body, since excesses or deficiencies can cause illness.

Normally the pituitary gland, a small gland at the base of the brain, regulates adrenal hormone production by secreting its own substance that signals the adrenal gland to increase or decrease its corticosteroid hormone-producing activity. Excess production of corticosteroid hormones, or hyperadrenocorticism, is usually caused by a tumor in either the pituitary gland (most common) or of the adrenal gland. In the common "pituitary dependent" form, the pituitary gland tells the adrenal gland to make more cortisol than is needed. In the less common "adrenal dependent" form, the adrenal gland does not listen to any signals and simply keeps making cortisol of its own accord. Usually, the pituitary dependent disease is caused by a benign growth of the pituitary gland. On the other hand, adrenal dependent disease can be due to either benign or malignant (cancerous) growth of the adrenal gland.

Very similar symptoms occur with "iatrogenic hyperadrenocorticism", where cortisone or cortisone-like medications given to a patient produce all the same signs of hyperadrenocorticism. In this situation the body's own pituitary and adrenal glands are not at fault, but the same effects occur because cortisone-type injections, tablets/pills, or topical medications have the same effects on tissues as the body's natural adrenal hormones. Such medications are commonly used for treating medical conditions including skin diseases; immune-mediated disorders including certain types of anemia, joint disease, liver disease, or neurologic disease; certain types of cancer such as lymphoma; and many others. Avoiding iatrogenic hyperadrenocorticism is one of the reasons recheck examinations, periodic blood testing, and possibly other tests are recommended when pets are taking cortisone-type medications. Corticosteroids are powerful hormones that affect almost all systems of the body, including the skin, bones, muscles, reproductive system, and immune system. They are frequently used in therapy because of their potent antiinflammatory effects.

When hyperadrenocorticism occurs unrelated to steroid medications, it usually affects middle-aged to older dogs (cats can get it too, but that is very rare). Symptoms vary considerably from one dog to the next and depend upon the level of hormone overproduction and duration of the condition. Drinking and urinating more than normal is the most common sign, especially when it cannot be accounted for by other circumstances like warm weather. Muscles may shrink, and the pet may show weakness as a result. Muscle weakness and an enlarged liver can cause a pendulous abdomen (pot-bellied appearance). Skin changes can include a very thin haircoat or hair loss, blackheads, hard plaques due to mineral deposits, a darkening of the color of the skin, and thin, fragile skin. Non-neutered pets may develop atrophy of the testicles (male) or failure of normal heat cycles (female). Obesity, panting, and repeated urinary tract infections are other signs that are sometimes present. It is common for pet owners and family members to think

that a dog with hyperadrenocorticism is just "getting old" as the dog develops these symptoms, when in fact, successful response to treatment can show that the symptoms are reversible and age was not the problem.

Routine blood tests and specialized confirmatory tests are warranted in patients showing symptoms of this sort because many other completely different diseases (such as diabetes and others) can cause similar symptoms. Routine lab tests, including a complete blood cell count, blood biochemistry profile, and urinalysis, will typically show some nonspecific changes in affected pets, and these tests are appropriate as a first line of evaluation to eliminate the possibility of other conditions. A screening test may require you to collect a urine sample from your dog at home. A series of specific tests designed to measure the response of the adrenal glands to the administration of hormones is needed to make a definite diagnosis. These tests are simple blood tests, but since they measure the adrenal gland's response over time, it is usually necessary to leave a dog in the hospital for several hours or the whole day for the two to three blood samples that need to be drawn during these tests. Based on these results, a treatment plan should be possible. However, in some individuals, the results of confirmatory tests are ambiguous and require abdominal x-rays, abdominal ultrasound, or MRI or CT scans to identify whether a tumor can be seen directly in the adrenal glands or in the pituitary gland (brain). These advanced tests are needed in some, but not all, dogs with hyperadrenocorticism.

## LIVING WITH THE DIAGNOSIS

Treating hyperadrenocorticism can make an affected dog's life better, but it is not always necessary to make life longer. Some pets with mild signs might not yet need treatment. On the other hand, dogs that urinate excessively, pant incessantly, have skin problems or weakness, or other worrisome signs will benefit from treatment. Usually, treatment consists of lifelong oral medications given by you to your dog every day or every few days, and periodic rechecks with the veterinarian. An exception is pets with hyperadrenocorticism caused by an adrenal tumor, where the treatment might be surgical removal of the tumor and the affected adrenal gland. Untreated, hyperadrenocorticism becomes progressively worse over months to years.

## TREATMENT

If your pet's hyperadrenocorticism is caused by administration of corticosteroid (cortisone-like) medications for a chronic condition, other treatment options must be found to allow the reduction or elimination of the corticosteroid treatment. It is important to not stop the corticosteroid medication suddenly, because the body typically has adjusted to it and abrupt termination can cause a pet to feel ill or, rarely, could produce life-threatening symptoms. Rather, you should discuss a time frame with your veterinarian during which you can taper the dose gradually before stopping.

If your pet's hyperadrenocorticism is caused by an adrenal tumor (as is the case in about 15% of dogs with hyperadrenocorticism), surgery to remove the tumor may be the treatment of choice. This is a surgical procedure performed while your pet is under general anesthesia. Adrenal tumor removal is a delicate and often challenging surgery, and in some cases the tumor may be found to be inoperable if it has intertwined itself around vital structures like the caudal vena cava or other essential organs. After successful adrenal tumor removal, you will need to give your pet corticosteroids orally

(tablets, which can be given with food, but be sure the food with the tablet is swallowed first before the rest of the meal to ensure the tablet was swallowed) for several weeks. The remaining adrenal gland will be shrunken and inactive, so this type of supplementation is necessary for several days to a few weeks until it gradually becomes fully functional again.

If your pet's hyperadrenocorticism is caused by a pituitary tumor (as is the case for most) or by an adrenal tumor that is inoperable, then lifelong treatment with antiadrenal medications may be necessary to control symptoms. The goal of treatment is to suppress the excessive production of corticosteroid hormones by the adrenal glands, but without going too far. Corticosteroids, in appropriate amounts, are essential to life. Therefore, the medication dosage needs to be tailored to each individual over days to weeks, in order to find a balance between suppressing the excess corticosteroid production without depriving the body of a normal amount of corticosteroid.

Several antiadrenal drugs are available, and the most common are trilostane (Vetoryl) or mitotane (also called Lysodren, or o,p'-DDD). Trilostane is approved for use to treat hyperadrenocorticism. Capsules should be given by mouth with food once or twice a day, every day. Your veterinarian will need to check that the dose is suppressing cortisol enough, but not too much, by conducting special tests. Timing of these tests is key and should be done the same number of hours post-pill each time the test is repeated. With mitotane, a higher (loading) dose is given for the first several days to decrease adrenal corticosteroid production. During this time, you need to monitor your dog closely at home. Important parameters to monitor include appetite, which should decrease from hearty/ravenous to adequate, but not disappear altogether; water consumption, which likewise should be visibly reduced in response to treatment but not stop completely; and alertness and general energy level, which should not change. Signs of sluggishness, weakness, or general loss of energy can indicate oversuppression of cortisol; call your veterinarian to discuss the best way to do this if any of these abnormalities becomes apparent. After your pet's condition has been brought under control, the mitotane dose will be reduced to a maintenance level. Your veterinarian can tailor the choice of treatment to your dog's specific case. Your home care will need to include monitoring at least twice a day for the symptoms described above, since these are potential signs of intolerance to the medication and should be addressed with a dosage change in consultation with your veterinarian.

Overall, complications of treatment can be indicated by apathy, weakness, lack of appetite, vomiting, or diarrhea. If these signs occur, call your veterinarian without delay and do not administer more of the antiadrenal drug until instructed to do so. If these symptoms occur, you may have been provided with a medication, prednisone, for this exact situation. If that is the case, you should administer the prednisone as prescribed. In most cases, such symptoms are caused by an excessive suppression of corticosteroid production, and withholding the antiadrenal drug as directed by your veterinarian can allow the adrenal glands to resume their natural production of corticosteroids.

## DOs

- Realize that many, very different diseases produce symptoms that are identical to the symptoms of hyperadrenocorticism.

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Therefore, correctly determining whether hyperadrenocorticism is present or not in your pet requires a series of specific tests that are aimed at making sure that the condition is identified properly and the best medication chosen.

- Give all medication exactly as directed.
- Monitor water consumption and appetite as indicators that antiadrenal treatment is working (water consumption and appetite should decrease somewhat). A complete lack of appetite or refusal to drink may be a sign of excessive antiadrenal drug treatment and warrants a phone call to the veterinarian.
- Understand that hyperadrenocorticism is more likely to negatively impact the quality of life for a dog than the length of life.

## DON'Ts

- Don't skip recommended recheck appointments. It is vital that the efficacy of the drugs be checked to make sure that there is not excessive suppression of adrenal hormone production.
- If your pet requires maintenance corticosteroid replacement therapy, do not discontinue treatment or miss doses. Your pet is completely dependent upon the medication and cannot survive without it.

## WHEN TO CALL YOUR VETERINARIAN

- When giving mitotane, lack of appetite or other signs of illness should be reported to your veterinarian promptly, because the dosage may need to be reduced, or a different drug substituted instead.
- If any of the signs listed below becomes apparent.

## SIGNS TO WATCH FOR

- Difficulty breathing, apathy, weakness, lack of appetite, vomiting, or diarrhea may indicate an emergency situation.

## ROUTINE FOLLOW-UP

- Periodic testing is needed to monitor response to treatment for hyperadrenocorticism. During the initial treatment period, testing may be needed every few weeks. After the dose has been adjusted to the maintenance level, the treatment should be monitored by laboratory testing every 4 to 6 months.

Practice Stamp or Name & Address