

# Hyperadrenocorticism

## ABOUT THE DIAGNOSIS

Hyperadrenocorticism, also called Cushing's disease, 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 of dogs, cats, humans, and most mammals. 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 either of the adrenal gland or the pituitary gland. This occurs either directly (with an adrenal tumor, which itself overproduces corticosteroids) or indirectly (with a pituitary tumor, which overproduces the substance that functions to signal the adrenal gland to make more corticosteroid hormones), with the majority of cases occurring as a result of indirect, or pituitary-based, overproduction.

A similar situation occurs with iatrogenic hyperadrenocorticism, where cortisone or cortisone-like medications given to a patient produce the symptoms 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 or tablets/pills have the same effects on tissues as the body's natural adrenal hormones. Such medications are commonly used for treating medical conditions including pruritic (itch-inducing) 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, it usually affects middle-aged to older dogs; cats very rarely have hyperadrenocorticism. Symptoms of hyperadrenocorticism vary considerably from one animal to the next and depend upon the level of hormone overproduction and duration of the condition. Drinking and urinating more than normal is a 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) in an animal that is not overweight. Skin changes can include a very thin hair coat, 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 paralysis of nerves in the face are other signs that are sometimes present. This group of symptoms seen in hyperadrenocorticism is called Cushing's disease or Cushing's syndrome. 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) may cause similar symptoms, and an accurate identification of the exact cause is essential for proper treatment. 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, immediately before heading to the veterinary hospital. For confirmation, 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 2 to 3 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

Lifelong treatment is needed for hyperadrenocorticism, and this consists of 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 is 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, surgery to remove the tumor is 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 vital 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 or by an adrenal tumor that is inoperable, then lifelong treatment with drugs that suppress the adrenal glands is necessary. The goal of treatment is to suppress the excessive production of corticosteroid hormones by the adrenal glands, but without going too far. Corticosteroids are essential to life, but in appropriate amounts. 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 mitotane (also called Lysodren, or o,p'-DDD), trilostane (Vetoryl), and ketoconazole. 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 that the current dosage of mitotane is excessive and should be reduced; 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. Trilostane and ketoconazole are alternative treatments for hyperadrenocorticism that are more recently recognized and may be preferable to mitotane in many cases. 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. Do not administer more of the antiadrenal drug until instructed to do so (typically, no more antiadrenal drug for several days at least). 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. Once this has occurred, which typically takes a few days, then the antiadrenal drug (mitotane, trilostane, or ketoconazole) can be restarted carefully at a lower dosage in order to control the exuberant adrenal corticosteroid production that inevitably returns when hyperadrenocorticism is present.

Cats with hyperadrenocorticism do not respond as well to antiadrenal medications as do dogs. Surgery often is preferable in cats with hyperadrenocorticism due either to pituitary tumors or adrenal tumors. Removal of both adrenal glands prevents the overproduction of corticosteroids due to a pituitary tumor, but the cat is then dependent on you for corticosteroid replacement medications (in pill form) for the rest of his/her life. Animals cannot survive with a complete lack of corticosteroids. Surgical removal of the pituitary tumor has been described in cats and may become the treatment of choice in the future, but currently it is extremely challenging and carries extensive risks.

## DOs

- Realize that many, very different diseases produce symptoms that are identical to the symptoms of hyperadrenocorticism. 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.
- Give a dose of prednisone if you suspect your pet is not tolerating mitotane treatment.
- 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 the sign of excessive antiadrenal drug treatment and warrants a phone call to the veterinarian.

## DON'Ts

- 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.
- Conversely, do not give high-dose prednisone (or similar corticosteroid-like drugs) all the time during treatment with mitotane/trilostane/ketoconazole because one will negate the effects of the other. Low-dose prednisone may be prescribed for part of the treatment time for some dogs; be sure to check with your veterinarian about *any* pills or injections for the skin or for arthritis, as many of these contain cortisone and can be counterproductive.

## 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

- Apathy, weakness, lack of appetite, vomiting, or diarrhea may indicate an adverse reaction to mitotane and possibly 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 6 to 12 months.

Practice Stamp or Name & Address