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Dog Tips

# When Your Dog Does These Things She Could Be Screaming, 'I'm Sick!'

She could be silently suffering from this disease. But if you're not paying attention, you could miss its preliminary hints. The disease is incurable, and your only hope of managing or reversing its early symptoms is to catch it early. What to discuss and diagnose with your vet.

#### Analysis by Dr. Karen Shaw Becker

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#### **STORY AT-A-GLANCE**

- Cushing's disease, also called hyperadrenocorticism, is a condition primarily of dogs involving the chronic release of too much cortisol by the adrenal glands
- An overproduction of cortisol is called typical Cushing's disease, and can be either adrenal dependent, or more commonly, pituitary dependent; "atypical" Cushing's involves the overproduction of aldosterone or sex hormones
- Cushing's syndrome can produce a variety of diverse symptoms, including increased thirst and urination, hair loss and weight gain around the abdomen
- Risk factors for atypical Cushing's appear to include early spaying and neutering, and exposure to xenoestrogens and other external estrogen mimics
- It's crucial to catch signs of Cushing's early, before it becomes full-blown. Many pre-Cushing's patients can be successfully treated with nutraceuticals, Chinese herbs, homeopathics, nutritional therapy and lifestyle management (reducing biologic stress)

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Cushing's disease is named for Dr. Harvey Cushing, who originally diagnosed the syndrome in a human in 1932. In veterinary medicine, the condition is most often seen in dogs, especially Terriers, Poodles, Dachshunds and the American Eskimo/Spitz. The disorder rarely occurs in cats.

The medical name for Cushing's is much more descriptive of the condition: hyperadrenocorticism. Hyper means "too much," adreno refers to the adrenal glands and corticism refers to a syndrome involving the hormone cortisol.

Hyperadrenocorticism, loosely translated, means "too much cortisol released by the adrenal glands."

# **The Fight or Flight Hormone**

Cortisol is known as the "fight or flight" hormone. In a healthy dog's body, cortisol is released by the adrenal glands intermittently, in small amounts. It's released in response to perceived stress and the possibility the dog might have to do battle or run for his life.

However, if for some reason your dog's body up-regulates its demand for cortisol, the adrenal glands begin overproducing the hormone, which can lead to a state of toxicity.

When cortisol is released by the adrenal glands, it triggers a release of glucose from the liver. Glucose provides energy to the cells of the muscles used to fight or take flight. A release of cortisol doesn't just trigger a release of glucose and energy to muscles, however.

This powerful hormone impacts a number of other important functions in your pet's body, including blood pressure, electrolyte balance, bone and fat metabolism and immune function.

# **Too Much of a Good Thing**

Your pet needs cortisol in small amounts, however, if she experiences chronic stress, her adrenals will release too much in response.

The body makes no distinction between good and bad stress. Your dog has the same physiologic response to a romp in the park (good stress) as she does to a cancerous tumor (bad stress).

Chronic stress leads to persistent over-secretion of cortisol, which can result in a number of serious disorders, including:

- Elevated blood sugar, which can lead to diabetes
- Thinning of the skin and coat
- Elevated blood pressure, which can result in heart and kidney disease
- Decreased muscle and bone mass
- Extreme hunger from burning all that extra glucose
- Increased risk of infection

An animal who chronically overproduces cortisol has compromised immune function. She can develop an infection

anywhere in the body. Infections of the gums, eyes, ears, skin and urinary tract are common.

If your dog has recurrent infections or an infection she can't seem to get rid of, it's possible too much cortisol is to blame.

## **Types of Cushing's Disease**

There are a few different forms of hyperadrenocorticism, and if your pet has the disease, it's important to know which type of Cushing's he's dealing with.

The adrenals are a pair of small, fat-covered glands located in front of the kidneys, and are composed of three layers. The outer, superficial layer is called the zona glomerulosa; the middle layer is the zona fasciculata; and the deepest layer is the zona reticularis.

The form of Cushing's your pet has depends on which layer of the adrenals is over-secreting hormones. If the middle layer (zona fasciculata) is overproducing glucocorticoids (also called steroids, cortisol and cortisone), it means he has "typical" Cushing's disease.

Typical Cushing's is either adrenal dependent or, much more commonly, pituitary dependent. About 85% of dogs with Cushing's develop the pituitary dependent form, in which the pituitary gland sends too much stimulating hormone to the adrenals. The adrenal glands respond by over-secreting cortisol.

In the remaining 15% of adrenal dependent Cushing's cases, a tumor develops in an adrenal gland and triggers an upregulation of cortisol production in the dog's body.

It's not uncommon for veterinarians to unintentionally trigger typical Cushing's by prescribing a too-high dose of oral prednisone (synthetic cortisone), or a course of prednisone therapy that is too long in duration. If your pet has taken prednisone for any length of time, he's predisposed to Cushing's disease.

"Atypical" Cushing's occurs when the outer layer of the adrenals (zona glomerulosa) overproduces the hormone aldosterone. Aldosterone balances the electrolytes in your pet's body. Atypical Cushing's disease can also result if the innermost layer (zona reticularis) begins overproducing sex hormones such as estrogen, progesterone (or rarely, testosterone) precursors.

#### Symptoms of Cushing's Disease

In excessive amounts, cortisol can create a host of diverse symptoms. Most dogs have a few, but not all of the symptoms of the disorder unless diagnosis comes very late in the course of the disease. The symptoms most commonly seen in dogs with early Cushing's include:

- Increased thirst and urination, which can lead to incontinence •
- Bruising ۲
- Increased panting ۲
- Hair loss •
- Abdominal weight gain (pot belly appearance), despite a reduction in calorie intake
- Irritability or restlessness
- Thinning skin and change of skin color from pink to grey or black •
- Much less commonly, rear limb weakness and blood clots  $\bullet$

Cushing's syndrome is so diverse because every inch of your pet's body contains cortisol receptors. That's why it's often a suppressed immune system that prompts the first veterinary visit.

If, for example, your pet has a recurrent urinary tract infection (UTI) or one that she can't get rid of, along with one or two other symptoms — perhaps thinning skin or a pot-bellied appearance, you should ask your veterinarian about Cushing's as a possible cause.

In my experience, many Cushing's dogs are misdiagnosed with liver disease. The liver of an animal with hyperadrenocorticism gets overtaxed from trying to process the excess cortisol circulating through the body. This causes an elevation in liver enzymes.

It isn't uncommon for veterinarians to stop looking once they see elevated ALT (alanine aminotransferase) and ALP (alkaline phosphatase), and diagnose liver disease when the problem is actually Cushing's that has secondarily elevated those liver enzymes.

# **Diagnosing Hyperadrenocorticism**

Unfortunately, many veterinarians tend to ignore repeated elevations in liver enzymes until several Cushing's symptoms are present, or a pet parent comes in complaining that their dog is suddenly urinating in the house or losing her hair.

The better, proactive approach is to try to prevent the disease from taking hold. That's why I recommend getting a copy of your pet's yearly bloodwork results. If your dog's liver enzymes are elevated, specifically ALP, ask your vet if your dog could be in the early stages of Cushing's disease.

The actual diagnosis of the disease is often challenging. It is typically done with blood tests like the ACTH stimulation (stim) test and the low-dose dexamethasone suppression test. Both these tests require at least two blood draws to compare cortisol levels for a definitive diagnosis of Cushing's.

When Cushing's is confirmed, your veterinarian will want to determine if it's pituitary or adrenal dependent. In my opinion, the best way to rule out an adrenal gland tumor is with a noninvasive ultrasound test. However, some vets prefer to do a third blood test called a high-dose dexamethasone suppression test.

Whichever method is used, it's important not only to establish a definitive diagnosis for Cushing's, but also to determine whether the form of the disease is adrenal or pituitary dependent. This information will help you and your vet decide on the best treatment options available for your sick pet.

If your pet has symptoms of Cushing's disease but you can't afford the expensive tests required for a definitive diagnosis, you can ask your veterinarian to do a urine test called the urine cortisol to creatinine ratio test, or the

UCC.<sup>1</sup> The UCC must be run using the first urine of the morning.

Results will help determine if your dog is excreting an abnormally high amount of cortisol in her urine. Since circulating levels of cortisol in healthy dogs are quite low, if there's a high amount of cortisol in your dog's urine, it's a solid clue that Cushing's may be present and further testing is warranted.

The UCC is also a less expensive way to rule out Cushing's. If your dog's urine cortisol is within the normal range, she most likely does not have typical Cushing's disease.

Another clue can come from a blood test called the Corticosteroid-Induced Alkaline Phosphatase (CiALP) test. Many dogs with adrenal disease have elevated ALP values. ALP can be elevated for a number of reasons, including bone, liver, gallbladder and adrenal disease.

The CiALP can determine what percentage of the ALP enzyme level is being caused specifically by the adrenal glands and is a simple, effective screening test to determine whether your pet is starting down the Cushing's path.

When I have a patient with an elevated ALP on routine bloodwork who is also exhibiting any symptoms of Cushing's, I use this simple test to determine if further diagnostics are warranted. In many cases, additional adrenal testing reveals elevated cortisol and estrogen levels but the dog still passes her Cushing's test.

Beginning a nontoxic treatment protocol to naturally manage her at this stage, which is called "pre-Cushing's Syndrome," is ideal in preventing progression of the disease.

Unfortunately, in the majority of cases, the disease is diagnosed only after full-blown Cushing's has developed and there's no holding it back. Once a dog has full-blown Cushing's, she will live with the disease for the rest of her life. It's a horrible illness that can be managed in many cases, but never cured.

#### **Treatment Options**

Most of the drugs currently available to treat Cushing's disease have many undesirable side effects. It's extremely important to discuss your concerns about possible side effects with your veterinarian. I recommend you do your own research as well. I try to avoid using Lysodren and other potent Cushing's drugs because in my opinion, the side effects are often worse than the symptoms the animal is dealing with. I usually catch the disease in my own patients before high drug doses are required.

If, however, your dog requires these drugs to manage full-blown Cushing's, I recommend starting with the lowest possible effective dose, and use it in conjunction with a natural protocol to reduce potential side effects. Identifying pre-Cushing's syndrome as early as possible and reducing your pet's risk for full-blown disease is the approach I always recommend. Dogs don't suddenly wake up with the disease — it happens over time.

Unfortunately, many conventional veterinarians ignore the early signs of adrenal dysfunction because they don't know what to do about it until a dog fails the ACTH stim test. The problem with this approach is it takes months and sometimes years for an animal to be officially diagnosed with Cushing's.

Waiting this long to take action often means waiting too long. I consider a dog to have pre-Cushing's syndrome when

he exhibits classic symptoms but is still able to pass the stim test. Often there are minor changes in bloodwork, for example, the UCC is borderline or slightly elevated, there are elevated cholesterol levels and/or the elevation in ALP has been proven to be cortisol induced.

I'm able to reverse many pre-Cushing's patients with nutraceuticals, Chinese herbs, homeopathics, nutritional therapy and lifestyle management (reducing biologic stress).

My advice is to be proactive by having your pet's ALP level checked annually. Ask your veterinarian to establish a baseline level and address any elevation from the baseline through a screening test like the UCC or CiALP to determine if your dog's body is over-secreting cortisol.

Having this information will help you better manage a pre-Cushing's situation before it develops to full-blown disease. And don't ignore symptoms. If your pet has consistent Cushing's-type symptoms, no matter how minor, they are absolutely worth investigating for a possible endocrine or adrenal disorder.

It's during the development of Cushing's disease that many dogs are also over-prescribed aggressive traditional drug protocols for full-blown Cushing's disease — with disastrous results.

When these potent drugs are prescribed for mild adrenal dysfunction, the result is often an acute Addisonian crisis in which there are insufficient adrenal hormones necessary for normal physiologic function. A natural protocol to manage pre-Cushing's is essential to avoid drug-induced hypoadrenocorticism (Addison's).

#### **Risk Factors for Atypical Cushing's**

As I mentioned earlier, atypical hyperadrenocorticism involves the outer and innermost layers of the adrenals and occurs when hormones other than cortisol are overproduced. The outside layer over-secretes aldosterone, the hormone that regulates electrolytes.

More commonly, the inside layer over-secretes sex hormones — most commonly estrogen and progesterone precursors. And although we don't know why animals develop atypical Cushing's, we do suspect certain factors may set the stage for the disease.

It's my belief early spaying and neutering definitely plays a role in up-regulation of sex hormone production by the adrenal glands. When a dog is desexed before puberty, which is generally around 6 months of age, the endocrine, glandular and hormonal systems have not fully developed.

Removal of the ovaries or testicles, and therefore all the sex hormones they produce, can become a significant problem later in life, because a dog's body requires a certain level of circulating sex hormones for normal biologic functioning.

When the sex hormone-secreting gonads are removed, the adrenal glands become the only source for them in the body. Over time, the adrenals begin to over-secrete these hormones to keep up with the body's demand. Interestingly, the same physiologic changes occur with ferrets that are desexed early in life, but not cats.

Not all veterinarians agree with me that desexing creates endocrine changes, and most conventional vets don't even think atypical Cushing's should be treated. Many also disagree on what to call these endocrine changes, and holistic veterinarians debate treatment protocols and frequency of monitoring.

I recommend letting common sense rule. If you have a dog whose quality of life is affected by elevated cortisol or sex hormone imbalances, address it and address it at naturally as possible, recognizing all drugs come with the potential for substantial unwanted side effects.

I always take action with symptomatic patients because there are many unpleasant consequences of hormone imbalances that can affect an animal's health, comfort and quality of life. It's common sense to assume that when critical organs like ovaries and testicles are surgically removed, there will be consequences. I believe atypical Cushing's is a consequence of early sterilization for many animals.

Re-balancing a pet's hormonal milieu results in not only physiologic improvement, but improvements in mental and emotional status as well.

The second factor that can upset hormone regulation in your pet's body is a substance called a xenoestrogen. Xenoestrogens are chemicals that mimic the effects of estrogen in the body. Because hormone disruption is a central feature of Cushing's disease, any substance that affects the body's hormonal balance must be evaluated.

Xenoestrogens are in fertilizers, pesticides, household chemical cleaning supplies, soil pollutants, nonorganic meats and plastics — including your pet's plastic food or water bowl. Your furry family member is exposed to as many external sources of estrogen mimics as you are. This exposure can negatively influence adrenal gland production of estrogens as well as your pet's endocrine balance.

If your pet has been diagnosed with atypical Cushing's, you should give some thought to his potential avenues of exposure to external estrogen-like compounds.

#### Natural Treatments for Atypical Cushing's Disease and Elevated Cortisol Levels

The late Dr. Jack Oliver, an endocrinologist at the University of Tennessee's College of Veterinary Medicine and an expert on atypical Cushing's, believed certain natural therapies could reduce the amount of circulating hormones in an animal's body.<sup>2</sup>

He advocated the use of melatonin, which is nontoxic, inexpensive, without side effects (when used correctly) and has shown to be effective in the early stages of the syndrome. Melatonin aids in the reduction of both estrogen and cortisol levels in the bloodstream.

In pets with elevated estrogen levels, Oliver also recommended high-lignan flax hulls, not to be confused with flax seed oil, which doesn't contain enough lignans. Lignans are phytoestrogenic, and they appear to send feedback to the adrenal glands to stop overproducing estrogen.

Oliver's methods have been shown to be quite effective in helping to manage, but not cure, atypical Cushing's in canine patients. **Holistic and integrative veterinarians** also use a wide range of glandular and homeopathic remedies, nutraceuticals (including DIM, diindolylmethane) and Chinese herbs to help manage their atypical Cushing's patients.

The disease has no cure, so one of the best things you can do for your pet is to find a veterinarian who is well-versed

in a variety of therapies known to have a positive effect on the syndrome.

# The Critical Importance of Identifying the Disease in Its Early Stages

Your dog is never perfectly healthy one day and suffering a full-blown degenerative or metabolic disease the next. Illness doesn't happen that quickly — it's a process. It exists on a continuum, and your pet is either headed toward health or away from it. If your veterinarian is reactive rather than proactive, you will very likely be told your pet is fine until she most definitely is not. Conventional vets tend not to address health in what I call the gray zone, in which there's a gradual progression of signs and symptoms that signal a disease in process.

Instead, they wait until your pet's condition has moved very clearly from the white zone of health to the black zone of disease. This is really unfortunate because there's enormous opportunity within the gray zone to slow down the march toward disease, and depending on the illness, to turn it around altogether.

If you believe your pet's health is changing and you're concerned about the development of Cushing's disease, ask your veterinarian to check for it.

At a minimum, he or she should measure your dog's baseline adrenal hormone levels using a qualified laboratory such as the Clinical Endocrinology Service at the University of Tennessee's College of Veterinary Medicine. The only way to effectively treat Cushing's symptoms naturally is to identify the syndrome early.

It is an easy matter to monitor bloodwork from one draw to the next to determine trends, changes and warning signs of an endocrine system disorder in the making. This is what your vet should partner with you to accomplish for the health of your pet. Identify every biochemical change in your pet's bloodwork that could signal an abnormality. Then dig as deep as necessary to confirm a diagnosis and put a treatment plan into action.

#### How to Help Prevent Cushing's in Your Pet

There are some common sense steps you can take to reduce your pet's risk of developing hyperadrenocorticism, including:

- Feed a moisture rich, balanced and species-appropriate anti-inflammatory diet to reduce biologic stress
- Minimize your pet's exposure to xenoestrogens
- Eliminate all grains and carbohydrates from the diet. Carbs trigger insulin release; insulin triggers cortisol release
- Investigate adaptogenic herbs and adrenal-supportive natural substances like magnolia (rhodiola), ashwagandha and phosphatidylserine
- Exercise your pet daily to help combat stress and promote the release of endorphins
- Address abnormal hormone levels early on with natural support, such as melatonin, DIM, glandular therapies and high-lignan flax hulls
- Instead of spaying or neutering, consider a sterilization procedure that leaves your dog's testicles or ovaries in place

#### **Sources and References**

<sup>1</sup> Journal of Small Animal Practice, Volume 38, Issue 3, March 1997, pages 99-102

<sup>2</sup> Steroid Profiles in the Diagnosis of Canine Adrenal Disorders, Dr. Jack W. Oliver, DVM, Ph.D.