

# Living with Cushing's Syndrome

*"At 11 years of age, Joujou had become a couch potato. She was drinking and urinating a lot. We thought she had a urinary tract infection and hypothyroidism. She was also starting to lose her hair. Blood work showed it was more than just that, and we were referred to an internal medicine specialist."*

*"Charlie turned 11 in July. We knew something was up for the past six months. He had excessive thirst and had lost 5 pounds. We had extensive blood tests, but the vet was unable to make a diagnosis."*

*"Kiki was 13 when she became very thirsty and urinated frequently. She often urinated inside the house despite being solidly house trained for many years."*

*"I have had two dogs diagnosed with Cushing's in the last 20 years. In Princess' case, the only physical manifestation was panting at inappropriate times — in a cool house while not physically active. A complete blood count showed elevated liver enzymes indicative that something was going on. We began doing more testing with Cushing's in mind, and she was diagnosed at 13 years old with a pituitary-dependent Cushing's."*

Your PBGV begins to drink more water and has to go out more often. These are symptoms that will lead to a visit to the vet, where complete blood work and urinalysis will be conducted. However, excessive thirst (polydipsia) and increased urination (polyuria) are symptoms that are seen in multiple disease processes. A physical exam and routine tests can determine if they are caused by diabetes, kidney disease, pyometra (uterine infection) or the use of certain medications. Once those possibilities are eliminated, further tests can be conducted to determine if the dog has primary liver disease or Cushing's syndrome.

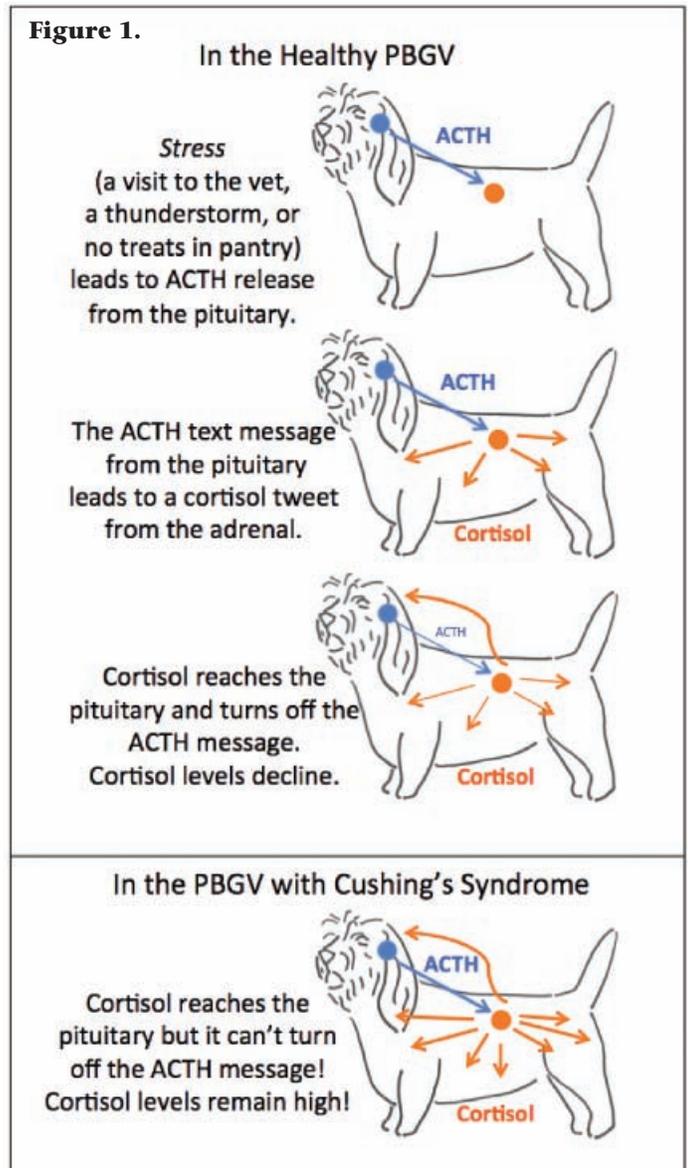
**What is Cushing's syndrome?** Cushing's is an endocrine disease caused by excessive secretion by the pituitary of a hormone called adrenocorticotropic hormone (ACTH). Unfortunately, Cushing's is not simple to diagnose because so many different organs can be affected. To understand the complexity of Cushing's, let us first look at the role of ACTH in the healthy dog.

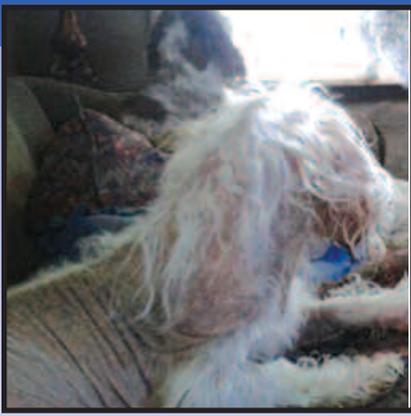
In a healthy dog, a stress causes the pituitary gland in the brain to secrete the hormone ACTH [see Figure 1 at right]. A hormone is a molecule that is secreted by a gland and transported throughout the body to deliver its message to other glands. ACTH delivers its message solely to the adrenal gland, informing it of the stressful situation. It is as if the pituitary has sent a private text message to the adrenal gland, which no other gland receives.

The adrenal gland does not keep this message a secret; instead, it spreads the message by secreting its own set of hormones, known as corticosteroids. The corticosteroids include both inflammatory hormones (aldosterones) and anti-inflammatory hormones (cortisol). Corticosteroids broadcast the stress message to multiple organs throughout the body. The private text message has become a very public tweet! This tweet tells the body to focus on surviving the stress rather than carrying out its normal metabolic functions. For example, cortisol calms the dog, turns off unnecessary physiological functions and prepares him/her to react to the stress. The pituitary also receives this tweet, recognizes that its text message has been received and shuts down further ACTH secretion.

**What causes Cushing's?** There are three major forms of Cushing's syndrome. More than 90 percent of cases in dogs are due to benign, slow-growing tumors in the pituitary. The tumors secrete high levels of ACTH in an unregulated manner [Figure 1]. The high ACTH stimulates the adrenal to secrete higher than

**Figure 1.**





Left: Two photos of Joujou before treatment, and, bottom, Joujou after beginning treatment for Cushing's syndrome. The photo bottom left shows the beginning of Joujou's new hair growth. Bottom center shows Joujou about 2 1/2 months on her maintenance dose of trilostane. She is doing great. She feels good, and has more hair than she ever had.



normal levels of cortisol. Unfortunately, the tumor's secretion of ACTH is not turned off by the cortisol so the text messages keep arriving telling the adrenal to secrete more cortisol.

Other cases of Cushing's are due to adrenal tumors that secrete cortisol even though they haven't received the ACTH text message from the pituitary.

Finally, the symptoms of Cushing's can also be induced by treatment of a dog with glucocorticoids for allergy, inflammation, autoimmune disease, or cancer.

In the end, Cushing's is a disease caused by too much corticosteroids. The clinical signs of Cushing's disease are largely due to the effects of the excess corticosteroids on multiple organs. In the liver, cortisol increases glucose synthesis and activates anti-stress and anti-inflammatory pathways. The resulting high blood glucose leads to insulin secretion from the pancreas, which causes increased fat synthesis and abdominal obesity. Muscle and skin weakens because cortisol leads to increased protein breakdown in those tissues. Cortisol also inhibits the secretion of vasopressin by the pituitary. Low vasopressin levels causes increased urine production, which leads to increased thirst. Cortisol also reduces bone formation, which cause osteoporosis in the long term.

*"Once Joujou was diagnosed she became ravenously hungry all the time and was drinking what seemed like gallons at a time."*

The first indications that a dog might have Cushing's syndrome are usually excessive thirst (polydipsia), increased urination (polyuria) and panting. Alopecia (hair loss) over the flanks, skin problems and increased appetite are other

common presenting complaints. An affected dog may also exhibit a drooping abdomen due to weakened abdominal muscles combined with increased fat deposition. The top two photos above show the severe hair loss and pot belly suffered by Joujou.

Cushing's syndrome is usually seen in older dogs, with a mean age at first diagnosis of 10.5 years. Onset is not easily noticed and is slowly progressive. It is seen in both males and females of all dog breeds, with an incidence of about one to two cases per 1,000 dogs per year. Analysis of more than 25,000 dogs evaluated over 15 years at the University of California-Davis Veterinary Medical Teaching Hospital shows that the incidence of Cushing's in purebred dogs is no greater than in mixed breeds. There is no evidence for inheritance of a predisposition for Cushing's in the PBGV.

*"I have had two dogs diagnosed with Cushing's ... both were picked up on routine screening. One dog was diagnosed at 13 and died of other causes at 15. The other was diagnosed at 12 years of age and is still with us at 17."*

**How is Cushing's diagnosed?** If Cushing's is suspected, a dog will typically be subjected to a complete blood count, serum biochemistry panel and urinalysis. Diagnosis is usually confirmed by measurement of cortisol in blood at various times after administration of a potent synthetic corticosteroid. In a healthy dog, the synthetic corticosteroid will suppress the ACTH secretion by the pituitary and subsequent cortisol secretion by the adrenal. A dog with a pituitary tumor will exhibit less suppression due to the synthetic corticosteroid, whereas a dog with an adrenal tumor will exhibit no *continued on next page*

## Glossary

**ACTH** – adrenocorticotrophic hormone is a protein secreted by the pituitary in response to biological stress. It binds to cells in the adrenal gland and leads to increased adrenal production of corticosteroids, such as cortisol.

**Cortisol** – a steroid hormone produced by the adrenal gland that circulates throughout the body. Its primary functions are to increase glucose synthesis, suppress the immune system, and increase metabolism of fat, protein, and carbohydrate.

**Endocrine** – relating to the collection of glands that secrete hormones into the circulatory system.

**Hormone** – a molecule produced and secreted by a gland, circulates throughout the body, and regulates the activity of distant cells or organs.

**Hyperadrenocorticism** – the syndrome of having excess adrenal hormones circulating in the body. Hyperadrenocorticism is also known as Cushing's syndrome.

## References

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**Cushing's** continued from page 27 suppression.

Unfortunately, this measurement of blood cortisol can be affected by the stress of spending a day in the hospital for repeated blood collections. For this and other reasons, cortisol is sometimes measured in urine, which can be collected at home. Complicating the diagnosis is the fact that older dogs may have one or more coexisting diseases that affect the results of the screening tests.

*"Kiki was diagnosed with both Cushing's and diabetes, which have similar symptoms. Adjusting the dosage of medications for each was complicated and did not bring Kiki's diseases under control. Possibly, if there had been only one significant disease the medication would have been more effective. We learned soon after those diagnoses that she had a third disease, hemangiosarcoma. This triple whammy was too much to deal with. She rather quickly became blind, which was probably a side effect of the diabetes. She became a very unhappy, uncomfortable dog that dragged herself around."*

Several PBGV owners found it challenging to have their dogs diagnosed because local veterinarians had little experience with the disease. They found it necessary to be referred to a tertiary care veterinary hospital for diagnosis and treatment.

**How is Cushing's treated?** It is important to determine whether the dog has Cushing's due to a pituitary or adrenal tumor because the treatments and prognosis differ. Magnetic resonance imaging or computerized

tomography scan may reveal the tumor and give additional information on prognosis. Less than 10 percent of Cushing's cases are caused by benign or malignant tumors of the adrenal. If benign, surgical removal of the adrenal will cure the disease. The prognosis is less favorable if a malignant tumor has spread beyond the adrenal.

The most common cause of Cushing's is a tumor of the pituitary gland. Surgery is not usually an option for this tumor, but it may be possible to control this form of the disease with medications that regulate the adrenal gland.

*Vetoryl* (Trilostane) was approved by the FDA in 2008 for use in dogs with Cushing's. This drug blocks the synthesis of cortisol in the adrenal without harming adrenal cells. It appears to be safe and effective, with minimal side effects that can include vomiting, lack of energy, diarrhea and weight loss.

*Anipryl* (Selegiline) is the only other FDA-approved drug for canine Cushing's; it is also approved to treat canine cognitive dysfunction. Anipryl blocks dopamine breakdown in the brain. The resultant higher dopamine levels inhibit ACTH synthesis in the pituitary. Unfortunately, only a fraction of dogs with pituitary tumors respond to Anipryl treatment.

Prior to approval of *Vetoryl*, the most commonly used drug was a human chemotherapy drug, *Lysodren* (Mitotane), which acts by destroying the adrenal cells that produce cortisol. *Lysodren* has severe side effects and was never FDA-approved specifically for dogs.

*"We had used Lysodren with my first dog with Cushing's. I had kept up on medications for the disease and was aware that Trilostane had become available. I told my vet that I wanted to treat Princess with trilostane. My vet had not heard of it and agreed to its use only under the supervision of a local veterinary internist who was using it in his practice."*

*"My first dog with Cushing's was treated with Lysodren. The second dog started on it but came very close to developing Addison's disease (cortisol levels too low) and has never been on medicine for Cushing's again. I have him tested every three to four months and, touch wood, he's been fine. All of my dogs get flaxseed, which has been recommended for atypical canine Cushing's."*

As pituitary-dependent Cushing's progresses, the pituitary tumor may grow large enough to cause neurologic symptoms, such as depression, circling, seizures and other behavior changes.

*"In March, Charlie had what I thought was a seizure. He was unable to stand and his body trembled, although he did not lose consciousness. This lasted about three hours, after which he appeared normal. He spent several days in the hospital having tests and an ultrasound, which I requested as I thought he might have cancer. He came home with no diagnosis. I now know that the seizure was a stroke caused by Cushing's. The following month, Charlie appeared mildly depressed so I took him back to the hospital. They suggested I wait and see. I requested a full thyroid panel be done, but it showed nothing. By June, Charlie had deteriorated quite quickly. I did a lot of searching on the computer and decided he had many symptoms of Cushing's. Armed with my paper work, I returned to the hospital and requested a Cushing's test. Charlie ended up with classic Cushing's symptoms: loss of coat, pot belly, bony head and altered muscle mass. He started taking trilostane in June."*

*"Joujou started on Trilostane and within a week, she became deathly sick with vomiting. We thought we were going to lose her. She was given Cerenia for the vomiting. Blood work was done*

every four weeks, and her dose had to be increased each time. Sadly, she had the same adverse effect each time the dose was increased. During this period, she had two urinary tract infections that we attribute to Trilostane affecting the immune system. There are other drugs available; however, this was the best for us because we are a multiple-dog family and with Trilostane you don't have to measure water intake. The disease is controlled now and Joujou is acting like a pup again."

"Through regular testing and tweaking of her medications, we felt we got Princess's test results where they needed to be. She seemed to suffer no ill effects, but remained healthy, active and alert. Nothing would have indicated she had such a syndrome. We had a couple of rough patches — once when she was diagnosed with pancreatitis. As we strictly watch food and diet, we felt it was due to the Cushing's being out of whack. We got the needed treatments and Princess never had another flare-up of pancreatitis, was not subject to multiple infections and maintained good weight."

**What is the long-term outcome for a PBGV with Cushing's?** PBGVs diagnosed with Cushing's are typically senior dogs that may have other health issues. Several PBGV owners described the cost of treatment.

"There is no doubt the disease has put a big dent in our pocketbook. There were monthly blood tests, at \$400 each, until her numbers were in the normal range. The trilostane is \$40 a month, obtained from a compounding pharmacy. When she needs Cerenia for vomiting, it is \$35 a day, unless a \$100 injection is needed. This disease easily runs into the thousands."

"I am not sure of Charlie's long-term outcome given his age

and severely compromised immune system. The cost of testing and treatment would also be prohibitive for a lot of people."

Princess's owner leaves us with these words of wisdom: "Get a good specialist who has treated the disease successfully before and has a good track record."

"Near the end of her life, Princess exhibited symptoms again. The last six months of her life (at age 18) became a guessing game. We were at the vet's office a lot and worked closely with them to keep her comfortable and going as long as we felt she wanted to. In the end, we never felt Cushing's took her from us, rather a combination of old age and her little body just wearing out. We have always felt that she was an awesome example of how a dog with Cushing's did not need to give up quality of life. She remained alert and with us until the end. As far as impact on her life or ours, we felt virtually nothing. Princess never stopped doing what she'd always done — she patrolled for vermin in the yard with her nose (aging did give her cataracts and diminished vision), barked to demand her chow at feeding times, cried for attention when she needed belly rubs. We changed nothing as we are not big travelers but are pretty much homebodies. We prefer to be on the couch with the kiddoes beside us. Pills were given at appropriate intervals and never a burden to administer.

"Princess was my once-in-a-lifetime love and I miss her to this day. I was honored to have her as a companion and confidante for 13 years. The thing I try hardest to convey to people facing Cushing's is that it is manageable. It is costly in the beginning, so the first year can be rough from a checkbook point of view, but after that regular testing can give you many years of good quality life and companionship." ■

**Delegate** continued from page 16 law school outreach program for future legislators and policy makers. The Canine Legislative Support Fund Educational Grants Program supports clubs' educational activities to advance responsible dog ownership and to protect future owners and breeders.

The AKC has a mission of being the leading authority for and voice of dogs. Breeders who follow parent club health testing recommendations will be identified on the AKC's website for people looking for a puppy. In 2013, the AKC had 20 million individual visitors, and 95 million page views, of which 3.2 million were the breeder classifieds. A subcommittee of the Parent Club Committee is pulling this project together.

Mr. Kalter reported that a proposal is being made to the board to televise the AKC/Eukanuba National Championship. Mr. Kalter congratulated the AKC's communication team for getting some very positive exposure on the "Today" show, and a video was shown to the delegates.

**President Report.** Mr. Dennis Sprung recognized the 25th anniversary of AKC's Canine Good Citizen Program. AKC's website WOOFipedia, launched a year ago, achieved 1.1 million unique visitors and 4.2 million page views in August. This site addresses younger people looking for information about dogs, and provides positive information about breeders and responsible dog ownership.

The National Owner-Handled Series is offered some 600 times in 2014 with many clubs seeing an increase in entries. Clubs offering the NOHS will receive assistance from the AKC promoting the event through emails prior to the show.

**CFO's Report.** Mr. Peter Farnsworth reported that revenue YTD is about \$38 million, about \$1 million down

from 2013, but expenses are lower than in 2013 so net operating profit is about \$4 million. Revenue related to core activities is steady, but revenue related to royalties, sponsorships and advertising are down. Personnel costs are down in 2014 because people who left have not been replaced. Investments equal about \$112 million. The AKC is investing in the development of new and easier services for us, including The Online Competition Management System, the Breeder Easy Registration, our website and outreach, and our Facebook presence.

Executive Secretary Jim Crowley read the proposed amendment to Chapter 14, Section 11 of "The Field Trial Rules and Standard Procedures for Retrievers." Mr. Timothy Carrion, delegate for the American Chesapeake Club, commented on the proposed amendment and said his club would be offering an amendment to the amendment read today.

Mr. Crowley read the names of three delegates who have served 25 years and congratulated the New Jersey Beagle Club for celebrating 100 years of AKC membership.

Mr. Crowley read the names of the nominating committee for candidates for the AKC Board of Directors, Class of 2019. Its written report has been received, and delegates will receive the names of the proposed slate within five days. Any delegate wishing to run by petition will have until Nov. 15 to submit the required 50 signatures to become a candidate. To date, candidates include Mr. Steve Gladstone, Mr. Carmen Battaglia, Dr. Tom Davies and Dr. Gregory Paveza.

Mr. Crowley reported that the Teller's Report for the AKC Delegate Committees isn't yet ready to be announced. The results will be announced during lunch. ■