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“The Great Pretender”



Learn about Addison's disease, which mimics symptoms of many other conditions, and can be fatal if not treated properly.

In June 1999, Booker, our 10-month-old Great Dane collapsed, again. Just four days previously, he was diagnosed with kidney disease. Hospitalization and fluids helped him immensely after that first collapse. He even had started eating again. What could be wrong now?

We took him back to the vet. This time, Booker was so weak he couldn't get up from the waiting room floor. The vet examined him there, but had no immediate answers. He asked us to leave Booker overnight for more tests and IVs. Reluctantly, we did.

Later that day the vet called with good news and bad news. The good news was that in consultation with specialists, he identified the problem as Addison's disease, an imminently treatable condition. And, the bad news? Addison's disease is a chronic health problem that will require a lifetime of management, including expensive medication and regular blood tests.

Addison's disease is the common name for hypoadrenocorticism, or adrenal insufficiency. The adrenal glands do not produce enough, if any, of a number of hormones, including aldosterone, which maintains sodium and potassium levels to regulate blood pressure (among other important functions), and cortisol, which helps the body metabolize glucose and deal effectively with physical and mental stresses of all kinds. It can occur with people as well as animals.

The two adrenal glands are located on top of each kidney, and are sometimes called the suprarenal glands. They are made up of two layers, the outer cortex and the inner medulla. The cortex secretes glucocorticoids, such as cortisol, and mineralocorticoids, such as aldosterone. The medulla area of the adrenal gland, part of the sympathetic nervous system, secretes epinephrine and is generally not affected by Addison's.

There are three types of Addison's

disease: primary, secondary, and atypical. Primary and atypical Addison's are usually the result of immune-mediated damage to the glands. Secondary hypoadrenocorticism

BY SHANNON WILKINSON

is failure of the pituitary to stimulate the adrenals with adrenocorticotrophic hormone (ACTH). It is most often a result of long-term corticosteroid therapy (i.e., prednisone), and also can be caused by tumors, trauma, or pituitary deformities.



Who gets Addison's?

Research shows that some breeds are more likely to have Addison's disease compared to other breeds. For instance, one study shows that West Highland White Terriers are six times and Great Danes seven times more likely to be affected by Addison's compared to all other breeds.

Another study indicates that Standard Poodles are nearly nine times, Wheaton Terriers nearly seven times, and Portuguese Water Dogs over 46 times more likely to be affected than other breeds.

The same studies also deter-

mined that Dalmatians, Pit Bull Terriers, Golden Retrievers, and a handful of other breeds are less likely to develop Addison's compared to all other breeds.

At the University of California, Davis, Professor Anita Oberbauer, Ph.D., is conducting research to determine if there is a genetic component to the disease, as indicated by the breed statistics. Information is being collected for Bearded Collies, Standard Poodles, Leonbergers, and Portuguese Water Dogs. According to

Booker, the author's Great Dane, was diagnosed with Addison's disease when he was just 10 months old. With scrupulous care and a whole, raw food diet, he stays healthy and strong.

Dr. Oberbauer, "The data we have for the beardies suggest a polygenic mode of inheritance without a confirmed major gene present." The data for the Standard Poodles also suggest a polygenic mode of inheritance but, "with a single locus/gene of large effect." However, she qualifies that

they aren't aware of definitive breeding of affected Poodle to affected Poodle, as a result there are not yet any data to show that it is indeed a single gene.

Interestingly, some studies have found that 70 to 85 percent of dogs with Addison's disease are female, and that the dogs affected are most often between four and seven years old. However, Addison's disease should be suspected any time the classic symptoms are seen, regardless of the dog's age or sex.

Symptoms

One of the difficulties of properly diagnosing Addison's disease is the common waxing and waning of symptoms. Karen Ivin, DVM, says that she always considers testing for Addison's disease with dogs who "have their ups and downs. When they aren't quite right, but aren't all the way sick either."

Dr. Ivin has a small, housecall-oriented holistic practice in Gilbert,



Any dog with symptoms of the disease should be tested. Tyler, the author's male Boxer, was diagnosed with Addison's when he was 14 months old, despite being the "wrong" age and sex for the disease.

Arizona. Although Addison's is often described as "rare," she is treating several dogs with Addison's disease, and has always had a couple among her clientele at any given time. She thinks that any vet who doesn't have at least a couple of dogs with Addison's in their practice just isn't seeing it. According to the pharmaceutical company Novartis, "a typical practice with two veterinarians who each see 1,500 dogs per year should expect to diagnose one case of adrenal insufficiency each year on average."

Symptoms can be subtle and often mimic those common to many other diseases. Typical symptoms include: depression or lethargy; anorexia; weight loss; vomiting; shaking or trembling; weakness; and diarrhea. Often the dog may experience episodes, such as vomiting or weakness, that resolve with fluids or perhaps even a dose of steroids. Unfortunately, the symptoms usually return.

This was our experience with Tyler, our second dog. We adopted Tyler, a Boxer, in June 2001, at eight months old. He was extremely thin and had regular bouts of diarrhea. After a stay with caregivers over Thanksgiving in 2001, he developed bloody diarrhea. Because of our experience with Booker we had Tyler tested for Addison's disease. Good news, his results were negative. Three months later, though, after Tyler vomited four times in two days, we had him tested again. This time, the results were positive for atypical Addison's. Note that neither of our Addisonian dogs were female or between four and seven years old at the time of the onset of the disease!

Diagnosing Addison's

Both dogs' diagnoses of Addison's disease were confirmed by the only definitive diagnostic tool, the ACTH response or stimulation test. In this test, blood is drawn to determine

Novartis Ceases Sales to Online Pharmacies

Until recently, some owners of Addisonian dogs bought their medications from Internet veterinary pharmacies such as MyPetPrescriptions.com, where the medications were available (with a prescription from a vet) at a lower cost than some veterinary clinics charge. However, Novartis, maker of the medication Percorten-V, has ceased the sale of its products to online pharmacies.

A Novartis spokesperson released a statement that explained in part, "Novartis maintains a strict policy of selling its products only to licensed veterinarians because we believe it is in the best interest of a pet's health that our medication be dispensed within a direct, veterinarian-client relationship.... Novartis products are available from most licensed veterinarians across the country, consistent with Novartis' long-standing sales policy of selling its products only to licensed veterinarians.

"If any pet owner who has purchased Novartis products through an Internet site has questions about this or any other Novartis product and how it can be purchased in the future, please contact Novartis Customer Relations at (800) 332-2761.

We would add that dog guardians should negotiate with their veterinarians for minimally marked-up prescriptions.

baseline cortisol levels. The animal is injected with ACTH. After approximately one hour, blood is drawn again to measure cortisol levels.

A dog with healthy, normal adrenal glands will have a baseline cortisol reading of between 1- 4 micrograms/deciliter. The cortisol level should be significantly higher, in the range of 6 - 20 micrograms/deciliter, post-stimulation. If resting cortisol is low and the dog has no or a low response to the stimulation, the diagnosis is Addison's disease.

Certain values on blood test results also may indicate Addison's as a possibility. This includes elevated potassium (hyperkalemia), low sodium (hyponatremia), low sodium to potassium ratio (Na/K), anemia, azotemia or uremia (high levels of nitrogen), eosinophilia (elevation in white blood cells called eosinophils), lymphocytosis (elevation in white blood cells called lymphocytes), elevated liver enzymes (ALT/AST), and urine specific gravity less than 1.030.

Conventional treatment

The conventional treatment for Addison's, like hypothyroidism or diabetes, is to replace the missing hormones. With primary Addison's disease, both mineralocorticoids and glucocorticoids must be replaced. Atypical and secondary Addison's require replacing only the glucocorticoid.

There are two medications available for the replacement of the mineralocorticoid, aldosterone, and both of these medications help the body keep sodium and potassium at normal levels. The first, fludrocortisone acetate (brand name Florinef™), is given orally on a daily basis. The other option is desoxycorticosterone pivalate or DOCP (Percorten-V™), an injectable medication that is usually given every 25 - 28 days.

Fludrocortisone acetate or Florinef

is the mineralocorticoid of choice for people with Addison's disease. Most people take one-half to two 0.1 mg tablets per day. However dogs don't metabolize the medication as efficiently and must start with doses of 0.05 - 0.1 mg of fludrocortisone per ten pounds of body weight. Some dogs require higher doses to regulate their electrolyte levels.

Florinef purchased from conventional pharmacies ranges in price from about 50 cents per 0.1 mg tablet

to close to a dollar per tablet. A 50-pound dog would require approximately five of the 0.1 mg tablets at a cost of \$75 to \$150 per month. However, there are lower-cost alternatives for fludrocortisone.

PetPharm, an Internet veterinary pharmacy based in Ontario, charges about \$35 Canadian for 100 tablets of Florinef. At the recent exchange rate, the cost in US dollars is less than \$23 per 100 tablets. At this price, medication for a 50-pound dog would cost about \$35 per month. While this makes Florinef much more affordable, if you have a large dog, you still contend with dosing multiple small tablets daily. (For more information about reducing the price of long-term medications, see "The Price of Prescriptions," WDJ September 2002.)

An alternative to purchasing the name brand tablets is to have the prescription customized into capsules, liquids, or flavored chews by a compounding pharmacist. Besides convenience, compounded medication can be significantly less expensive than its brand name equivalent. One compounding pharmacy, Tiffany Natural Pharmacy in Westfield, New Jersey, charges about \$45 for 100 0.5 mg capsules. That equates to just \$13.50 a month to treat a 50-pound dog with just one capsule per day.

There are fewer purchasing options for Percorten-V, the injectable medication used only for animals with Addison's. Many guardians take their dog in for his or her monthly Percorten injection, allowing the vet to test the dog's electrolytes if necessary, check for any weight changes, and monitor the dog's overall health and demeanor.

After time, though, the guardian may want to give the injection at home. This not only might save some expense, but may also decrease stress. Novartis, the maker of Percorten, recommends intramuscular



What
you
can
do...

- ❖ **Suspect Addison's disease, particularly if you feel your dog just isn't right, but vet(s) haven't come to any firm diagnosis.**
- ❖ **Shop around for less expensive medications. The initial financial burden can be overwhelming, but with some time and effort, lower cost medications may be available.**
- ❖ **Work with your vet. It's important to discuss any changes to medications, supplements and/or diet with your vet. If your vet isn't willing to listen, find one who will.**
- ❖ **Join an online support group. Talking to other animal guardians with Addisonian dogs can be invaluable.**

injections because that was the method used during the FDA approval process. However, a subsequent study published in the Journal of American Animal Hospital Association found that easier to give subcutaneous injections are just as effective.

Like Florinef, the dosage of Percorten is weight-dependent. The standard dose is 1 mg per pound of body weight. The medication comes in 4 ml bottles and there are 25 mg of the medication in each ml. Therefore, a 50-pound dog would require 50 mg or 2 ml of Percorten.

Percorten is available only from veterinarians and veterinary pharmacies. Prices vary widely, depending on the clinic or pharmacy markup. When Booker was originally diagnosed, we were charged \$60 for the first ml and \$40 for each ml thereafter. That would make the monthly injection for the 50-pound dog cost about \$100. However, I soon learned that the price included a greater than 100 percent markup.

We negotiated the price with our vet by pointing out that a dog with Addison's requires regular bloodwork and office visits in addition to the medication. (Dog owners may be unable to purchase Percorten from Internet pharmacies, even with their veterinarian's prescription, as they can with many other long-term medications. See sidebar, lower left.)

Amy Rogers' Rottweiler, Venus, was diagnosed with Addison's recently. Initially, her vet started Venus on Percorten injections and didn't even discuss the option of oral medication. However, Amy has recently switched Venus, under the watchful eye of her vet, from the injections to compounded fludrocortisone. This change will save Rogers about \$80 per month.

In addition to replacing the mineralocorticoids, dogs with Addison's disease need the glucocorticoid, cortisol, replaced as well. About 50 per-

cent of dogs require daily glucocorticoid supplementation, while all dogs with Addison's require glucocorticoid supplementation in times of stress.

Stress is individual. It can come in many forms – physical or emotional, good or bad. For instance, some dogs may require extra glucocorticoids for a visit to the vet, while other dogs may need them because of an extra long play session. While it is important to observe all dogs with Addison's closely, knowing each individual dog's stressors is crucial.

There are a number of glucocorticoids available to replace the cortisol that the adrenals are no longer producing. Most vets recommend using



When Amy Rogers' Rottweiler Venus was initially diagnosed, Amy was not given information on alternative medicines or therapies. With a little research, she learned she could save about \$80 per month on Venus' medications.

prednisone, while most people with Addison's take hydrocortisone. The other glucocorticoids used include prednisolone, methylprednisolone, and dexamethasone. These all tend to be inexpensive medications.

You may recognize prednisone as the steroid frequently prescribed

for allergic reactions, skin problems, or autoimmune conditions. However, its use with the Addisonian patient is at far smaller physiological doses, rather than the therapeutic doses often used for anti-inflammatory and other situations. The typical recommended dosage of prednisone is 0.1 - 0.2 mg per pound per day. That is 5 - 10 mg per day for a 50-pound dog.

However, many people find that on these doses their dog with Addison's shows undesirable symptoms such as excessive drinking and urination, increased appetite, infections, even behavioral changes. Because these dogs will be on medications for the rest of their lives, it is important to fine-tune the dosages to maximize benefits, while minimizing unwanted side effects.

If a dog suffers from side effects of prednisone, it might be worth trying hydrocortisone instead. That's what I found with Booker. He was on 15 mg of prednisone every other day. Yet he was unable to go more than four hours without urinating, was having recurring skin infections, and was balding on his face, chest, legs, and abdomen. After switching to hydrocortisone under the care of our vet, his dose was reduced significantly and these problems went away.

Of course, any of these medications require a prescription from your primary veterinarian. It is important, particularly with Addison's disease, that your dog is monitored closely through observation and blood tests. Always work with your vet when exploring changes in medications.

Complementary Therapies

According to most experts, there is no replacement for the conventional medications required to treat Addison's disease. However many believe that the quality of life can be improved and medications even reduced by using various supple-

ments, improving the dog's diet, and incorporating complementary modalities such as acupuncture and TTouch.

Booker is a perfect example of how complementary therapies can enhance conventional treatment. Months after diagnosis, Booker was clinically stable with excellent blood test results, but he was still experiencing a number of problems, such as digestion issues, skin problems, and low energy levels.

After incorporating a variety of complementary therapies including Western and Chinese herbs, TTouch, acupuncture, supplements, and a raw, whole food diet, his digestion is greatly improved and his energy level is higher than as a puppy. In addition, his medications have been reduced significantly. At the time of switching him to hydrocortisone, he was taking 30 mg per day. He now takes 7.5 mg per day. He also was receiving 6.4 ml

of Percorten-V every four weeks. This has been reduced over 65 percent to 3.2 ml every six weeks.

Many vets agree that diet is the key to a foundation of health for any dog. Before focusing his efforts on diet, Ian Billingham, BVSc, studied acupuncture and met with herbalists and homeopaths trying to determine what has the greatest impact on the health of our dogs. He learned that without a good diet, therapies such as acupuncture and homeopathy won't work properly.

Gloria Dodd, DVM, agrees. She believes that diet accounts for 70 percent of the treatment for an ill dog and this is the first change she encourages clients to make. Both Billingham and Dodd are proponents of a raw, fresh, whole foods diet designed for carnivores.

While Dr. Ivin recognizes the importance of diet in the overall health

and treatment of an animal, she doesn't believe it has to be raw, or even home-cooked. However, the commercial food must be of top quality.

One of the most frequently recommended complementary treatments for Addison's is also one of its original treatments: glandular supplementation. Before the discovery of cortisol, and later its synthetic analogs cortisone and prednisone, patients with Addison's disease were given ground-up or extract of adrenal gland. Now the process has evolved and a number of companies, such as Standard Process and Nutriwest, manufacture glandular products in tablet or capsule form.

"The addition of glandulars may sometimes help reduce the medication levels of my patients," says Dr. Ivin, "but they nearly always improve how the dog feels on a day-to-day basis." She says they help reduce

Glossary of Terms

Adrenocorticotrophic Hormone or ACTH — Hormone secreted by the pituitary that stimulates the adrenal glands to produce cortisol. Used to test adrenal function and diagnose Addison's disease.

Aldosterone — This adrenal hormone, a mineralocorticoid, is crucial to virtually every cell as it balances the electrolytes sodium and potassium.

Cortisol — This adrenal hormone, a glucocorticoid, is often referred to as the stress hormone. In addition to times of stress, the body normally secretes a regular amount every day. It impacts the body in a multitude of ways, including controlling fat, protein and carbohydrate metabolism and the inflammation response.

Desoxycorticosterone Pivalate — The active ingredient in Percorten-V.

Electrolytes — Mineral salts or chemical substances that conduct electrical current across and between cells. They

include sodium and potassium and are necessary for basic body functions.

Florinef™ — Oral medication used to replace the mineralocorticoid, aldosterone.

Fludrocortisone Acetate — The active ingredient in Florinef. It is available through compounding pharmacies.

Glucocorticoid — Hormones secreted by the adrenal gland, such as cortisol, which metabolize glucose and help the body deal stress.

Mineralocorticoid — Hormone secreted by the adrenal gland, such as aldosterone, which maintains sodium and potassium levels to regulate blood pressure and other functions.

Percorten™ — Injectable medication used to replace the mineralocorticoid, aldosterone.

Noel, A Study in Alternative Therapy

Noel is an eleven and a half year old Great Dane with Addison's disease. Lory Jenkins and her husband adopted her on Christmas Eve, 1991. She was malnourished, underweight, timid and very skittish in certain circumstances.

Noel flourished under Jenkins' care – she gained weight and confidence over time. In 1997 though, her energy level diminished, as did her appetite. Initial blood tests indicated early renal failure. She continued to lose weight, became more lethargic and finally quit drinking water.

Jenkins became desperate and started calling all the vets she could find. A homeopathic vet strongly suggested having Noel tested for Addison's disease. The ACTH Stimulation test was done – Noel had a very clear-cut case of Addison's.

She was started on Percorten-V and prednisone immediately and seemed to feel better the next day. These medications were continued over the next five years. In general, her health was good – her appetite was normal and her energy level was stable.

Over time though, Noel became incontinent and was placed on PPA (phenylpropanolamine). She also began having recurring bladder infections and was given numerous courses of antibiotics. The infections started reoccurring more quickly after finishing each course of antibiotics. Jenkins was concerned that one day Noel would develop an infection that couldn't be helped by antibiotics.

Jenkins was referred to homeopathic vet, Larry Bruk in early 2002. Bruk, a classically trained homeopath, doesn't treat a disease per se, but rather treats a patient based on the individual and the symptoms they are manifesting. Bruk's initial consultation with Noel and Jenkins took approximately two hours. He wanted details about everything from symptoms to preferences for hot or cold to changes during the day.

Based on this information Bruk selected a homeopathic remedy that fit Noel. Jenkins prepared the remedy and gave Noel one dose. Then the waiting and watching began. She reported her observations to Bruk. Bruk might wait longer, repeat the dose or select a different remedy based on the situation.

At the same time, Noel's dose of prednisone was transitioned to natural hydrocortisone from Pet Health Pharmacy. After time this was switched to adrenal glandular supplementation. Her dose of Percorten also was reduced.

At the end of several months, Noel's bladder infections had not recurred. She was taken off PPA and showed no incontinence. Plus, her Percorten dose had been reduced by more than half as she went from a 4.8 ml injection every 25 days to a 2.8 ml injection every 32 days. And, according to Bruk there is room for even more improvement.

At her last injection, Noel, under close watch and with several blood tests, went 53 days in between injections of Percorten. When she was given her last dose at the beginning of December, it was reduced again to 2.6 mls. Bruk believes that with time she may be able to go without conventional meds altogether because the homeopathic remedies are helping balance her energetic state so that she can heal herself.

fluctuations in the disease process, help keep the dogs stable, and decrease deterioration as they age.

Various herbs may be beneficial, including nutritive herbs that supply vitamins and minerals necessary for adrenal functions, such as dried nettle, dandelion, parsley, and spirulina; those that support adrenal function, like licorice and borage; those that help the liver, like milk thistle; and those that reduce the impact of stress, such as astragalus and ginseng.

The herb licorice has been reported to have a positive effect with Addison's disease. Research has shown that licorice helps prolong the activity of natural and synthetic corticosteroids like hydrocortisone, which may enhance the activity of medications or even allow dosage reductions.

Dr. Ivin uses Chinese herbal formulas with great success. Because, as with homeopathy, Chinese herbal remedies are prescribed on an individual basis, she may use a variety of formulas depending on the particular symptoms of her patient. Most of the formulas that she chooses contain the key ingredient, ginseng. Ginseng is an adaptogenic herb that helps the body adapt to environmental and emotional stressors and supports all the major systems of the body rather than having strong affinities for any one system or organ.

Since Addison's disease inhibits the body's ability to effectively deal with stress, reducing stress and keeping your dog's life stable is important. "Maintaining a low-stress, stable environment for your dog helps limit the necessary changes in medication," says Dr. Ivins. She has found that flower essences are helpful in reducing stress and limiting the need for extra glucocorticoids.

Acupuncture and chiropractic care may also be beneficial. Dr. Dodd believes strongly that in addition to medications, supplements, and diet, it is necessary to treat the imbalances in



Acupuncture is an effective complement to conventional veterinary treatment. Practitioners frequently find that they can reduce the medication a dog receives if he also receives acupuncture treatments.

the acupuncture energy flow meridians of the endocrine glands, digestive organs, immune system, and kidneys.

Post diagnosis follow-up

Immediately after diagnosis, and whenever any changes are made to medications or supplements, it is important to perform blood tests to ensure the dog is stabilized. The electrolyte levels offer the most specific information, particularly about the efficacy of the mineralocorticoids. However, thorough blood work including a full chemistry panel, complete blood count, and thyroid panel are helpful in determining the overall health of an animal.

Thorough management of an Addison's patient, and fine-tuning his medications and treatments to maximum effect can be difficult, especially with so many variables. Dr. Ivin encourages owners to work closely

with their veterinarians to understand the disease as much as possible. "There is no such thing as a dumb question," she says. Dr. Ivin also recommends keeping track of everything, including the dog's activity level. Without a written record, it is difficult to know the impact of changes made in medications, supplements, diet, or other therapies.

While managing Addison's disease can be daunting, it is not impossible. The greatest motive for working at it is the day-to-day health and longevity of your dog. Research shows that when properly stabilized, Addison's disease does not seem to impact the longevity of a dog.

Dr. Ivin recently lost a canine patient with Addison's this summer. The Australian shepard was diagnosed at about eight years old and died at 16. Now that is worth working toward.

Contacts and Sources:

Canine Genetic Analysis Project – Addison's Disease

For more information and to request a kit, go to: <http://cgap.ucdavis.edu>

Larry Bruk, DVM

Mill Valley, California, 415-381-0723
wholeanimal@earthlink.net.

Gloria Dodd, DVM

Gualala, CA, 707-785-9171
www.holisticvetpetcare.com

Karen Ivin, DVM

Desert Mobile Veterinary Services
Gilbert, Arizona, 480-497-6362.

International Academy of Compounding Pharmacists

800-927-4227, fax 281-495-0602
www.iacprx.org.

MyPetPrescriptions.com

c/o Medicine Man Pharmacy
Liberty Lake, Washington,
877-666-2501, fax 509-755-3337
www.mypetprescriptions.com.

Pet Health Pharmacy

Youngtown, Arizona
800-742-0516, fax 866-373-0030
www.careforpets.com

PetPharm, a division of Broadview Pharmacy

Toronto, Canada
888-423-9444, fax 888-423-7860
www.petpharm.org

Tiffany Natural Pharmacy

Westfield, New Jersey
908-233-2200, fax 908-233-3975

AddisonDogs.com

a non-profit organization that provides information and support to people caring for dogs with Addison's disease