

ADDISON'S DISEASE: UNCOMMON OR UNDERDIAGNOSED?

A roundtable discussion sponsored by an educational grant from Novartis Animal Health

Participants:

Ellen Behrend, VMD, MS, PhD,
DACVIM
Department of Clinical
Sciences
College of Veterinary Medicine
Auburn University
Auburn, Ala.

Catharine Scott-Moncrieff, MA,
VetMB, MS, MRCVS, DACVIM,
DECVIM, DSAM
Department of Veterinary
Clinical Sciences
School of Veterinary Medicine,
Purdue University
West Lafayette, Ind.

Deborah Greco, DVM, DACVIM,
MS, PhD
The Animal Medical Center
New York, N.Y.

Peter Kintzer, DVM, DACVIM,
Boston Road Animal Hospital
Springfield, Mass.

Moderator

David Bruyette, DVM, DACVIM
VCA West Los Angeles Animal
Hospital
West Los Angeles, Calif.

Dr. David Bruyette: The topic of our discussion today is Addison's disease. This condition can be problematic. Many practitioners struggle with the diagnosis—the signs mimic those of other diseases. And practitioners may not be testing for Addison's disease as often as necessary. Once the condition is diagnosed, what's the best way to manage it? We'll discuss all of those issues today.

Let's start with the first question. What is Addison's disease? Describe the signalment of animals presenting with this condition.

Disease classification and signalment

Dr. Ellen Behrend: Addison's disease is hypoadrenocorticism. We recognize two types. The first is typical Addison's disease (which is always primary disease). This type involves both glucocorticoid and mineralocorticoid deficiency. The second type, atypical Addison's disease, involves glucocorticoid deficiency alone. This type can be classified as primary or secondary disease with primary being an adrenal problem and secondary being a pituitary problem. The typical signalment? It's mostly a disease of young-to-middle-age dogs. The median age (depending on the study) is four to six years of age. But dogs younger than one year old and up to 12 years old have been reported to have the disease. In general, two-thirds to three-quarters of affected dogs are female. But in certain breeds, such as bearded collies and standard poodles, males and females are equally affected. Breed predilections include Great Danes, Portuguese water dogs, standard poodles, West Highland white terriers, bearded collies, and rottweilers.

Bruyette: Are there any other points about disease classification or signalment that are important for practitioners to know?

Dr. Catharine Scott-Moncrieff: Atypical Addison's patients are not always purely glucocorticoid-deficient. To me, atypical means that

they don't have the classic electrolyte changes. They don't have the typical hyponatremia and hyperkalemia, but they may still be mineralocorticoid-deficient, although their electrolytes don't reflect it.

Dr. Deborah Greco: That's a good distinction.

Bruyette: Of animals that are initially diagnosed with an isolated glucocorticoid insufficiency, what percentage develop electrolyte abnormalities over time that require mineralocorticoid supplementation?

Greco: In my experience, most dogs do.

Scott-Moncrieff: We try to determine if these cases involve primary or secondary disease. If they have primary Addison's disease, almost all of them develop electrolyte abnormalities. The secondary cases do not.

Dr. Peter Kintzer: I agree. Almost all dogs develop electrolyte changes, though it may take several months.

Greco: Or sometimes years.

Kintzer: If you follow patients long enough, they'll usually develop electrolyte abnormalities.

Bruyette: It's been my experience as well that most of them progress, although I've been amazed by how long it takes. Some dogs on initial evaluation may have low serum aldosterone concentrations, but for whatever reason, their electrolyte concentrations are still normal.

Let's discuss disease incidence now. Current estimates suggest that a practitioner will diagnose one to two cases per year. Does this number reflect the true incidence of the disease? If not, why?

Disease incidence

Scott-Moncrieff: There's been a huge



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Points to Consider

- Dogs with normal electrolyte concentrations can have Addison's disease.
- Addison's disease is underdiagnosed and more common than current estimates suggest.
- Dogs with Addison's disease often have nonspecific gastrointestinal problems such as anorexia, vomiting, or diarrhea.
- The waxing and waning signs of weakness and collapse—often associated with stressful events—are important clues to Addison's disease.
- A sick dog with a normal lymphocyte count suggests the dog might have Addison's disease.

increase in the recognition of atypical Addison's disease. If we searched for Addison's disease in the Purdue University veterinary medical database, I think we'd find a much higher number of dogs with atypical Addison's disease than expected. The current estimate that five percent of Addison's cases are atypical is lower than it should be. Few practitioners realize that dogs with normal electrolyte concentrations can have Addison's disease. This disease is much more common than current estimates suggest.

Greco: I agree. Before I came to the Animal Medical Center, I didn't look for the disease as often. At AMC, we look for it all the time, and we're finding a much higher incidence here than at other institutions.

Bruyette: I agree with both of you. If you're in a practice that has seen atypical Addison's disease, you're much more likely to do an ACTH stimulation test on a dog with vague signs and normal electrolyte concentrations. We're doing ACTH stimulation tests left and right in my practice because we've all found dogs with normal electrolyte concentrations and glucocorticoid deficiency.

Kintzer: You don't find Addison's disease if you don't look for it. It's as simple as that.

Scott-Moncrieff: It's interesting that the number of Addison's cases increases when the clinicians at Purdue who are really interested in Addison's disease are working in the clinics. Every resident gets fooled by one, and then he or she starts looking for and finding Addison's cases. In addition, whenever I give a presentation on atypical Addison's disease, several practitioners invariably tell me they intend to start looking for this condition or they've been working up a dog for months, and they think that's what the dog has. I think this disease is frequently undiagnosed.

Greco: Yes. I think the missed cases are often the dogs diagnosed with inflammatory bowel disease.

Scott-Moncrieff: Or they're diagnosed with nonspecific gastrointestinal disease or hepatic disease.

Kintzer: Another reason we see Addison's cases referred is a diagnosis of acute renal failure. We have a busy emergency service. I tell clinicians to check for Addison's disease before they euthanize a patient for acute renal failure.

Bruyette: We all agree that the incidence of Addison's disease is underestimated. Practitioners need to consider it more often.

Scott-Moncrieff: One more point—we've discussed that normal electrolyte concentrations don't rule out Addison's disease. Practitioners also need to remember that what's included in serum chemistry panels isn't necessarily standard. They may look at a panel quickly and see that it's normal. Then they realize that sodium and potassium concentrations weren't included. I think it's another way clinicians miss the diagnosis.

Clinical signs

Bruyette: Why don't we move on to the third question, which deals with the clinical signs. What are the typical clinical signs of animals with Addison's disease? Which findings from the patient's history and lab tests are suggestive of Addison's disease? We should address both the glucocorticoid- and the mineralocorticoid-glucocorticoid-deficient dogs.

Greco: The typical patient with Addison's disease shows signs of collapse and weakness and has a history of waxing and waning episodes of these signs. Affected dogs often have nonspecific gastrointestinal problems such as anorexia, vomiting, or diarrhea. The waxing and waning signs of weakness and collapse—often associated with stressful events—are important clues from the patient's history. If affected animals have electrolyte changes, they're quite sick and have clinical signs of collapse, bradycardia, and shock—the textbook classic Addisonian crisis.

Atypical cases are much more confusing because they respond to nonspecific therapy. For example, they may respond to fluid therapy or withholding food for a day. These cases can be challenging unless you have a high level of suspicion. I also evaluate the lab results—particularly the hematology findings. If these patients don't have electrolyte changes, I look for elevated or normal eosinophil and lymphocyte counts (lack of a stress leukogram), and possibly anemia, which can develop because decreased glucocorticoids depress RBC production. Of course, the classic electrolyte changes of hyponatremia, hypochloremia, and hyperkalemia, coupled with azotemia, should alert the clinician to the possibility of Addison's disease.

Scott-Moncrieff: Most patients have fairly severe clinical signs. They're in the intensive care unit and

are receiving intravenous fluids. I agree that the lack of a stress leukogram is an important clue. A sick dog with a normal lymphocyte count suggests the dog might have Addison's disease. Laboratory abnormalities typically seen with gastrointestinal disease—such as hypocholesterolemia, hypoproteinemia, and liver enzyme changes—may also suggest Addison's. If I see abnormalities like that on the panel, I like to rule out Addison's before pursuing gastrointestinal disease. Always make sure it's not Addison's before you anesthetize and perform endoscopy on these patients.

Greco: Or before putting them on prednisone.

Kintzer: The history often reveals that these patients have seen their veterinarians several times in the past few months for nonspecific gastrointestinal signs, and that they were treated with fluids and an injection. The injection almost invariably turns out to be a steroid—something that lasts for several days to weeks. Then they crash again.

Behrend: Dogs with Addison's disease can also have melena or hematemesis. Clinicians may see these signs and rule out Addison's disease. It's a small percentage of Addisonians that have melena or hematemesis, but it's certainly possible.

Kintzer: Approximately 15 to 20% of dogs with Addison's are reported to have melena.

Scott-Moncrieff: Five percent of Addison's cases can present with acute gastroenteritis resembling parvovirus infection or acute hemorrhagic gastroenteritis. This is an unusual manifestation, but it's important to consider Addison's disease in affected animals.

Greco: And, as mentioned previously, dogs can also present with clinical signs and laboratory abnormalities suggestive of acute renal failure.

Kintzer: Most of these cases don't look prerenal because the urine is not concentrated. That's what fools most of the veterinarians who refer them for renal failure. Practitioners forget that a large percentage of Addisonian dogs won't have concentrated urine, so the condition looks like primary renal disease when it's not.

Scott-Moncrieff: And an occasional case will present with hypoglycemic seizures as well.

Bruyette: All good points. We've touched on the

next question but let's discuss it in more depth. What are the most common differential diagnoses for Addison's disease?

Common differential diagnoses

Scott-Moncrieff: As we've discussed, animals presenting with nonspecific signs of gastrointestinal disease are the biggest group. Another group would be animals with signs of liver disease. They have increased liver enzyme activity, hypocholesterolemia, and hypoproteinemia. Other groups include animals that look as though they have acute renal failure with azotemia and inability to concentrate their urine, and animals that present with hypoglycemia so they may look like an insulinoma case. But the most common would be dogs with nonspecific gastrointestinal signs. Think about Addison's disease in those cases.

Kintzer: I'd agree. The only thing I might add is Addisonians that are hypercalcemic. That may add a few conditions such as hyperparathyroidism and hypercalcemia of malignancy to the list as well.

Scott-Moncrieff: The occasional dog with an additional endocrinopathy can also confuse the issue.

Greco: Such as hypothyroidism.

Testing protocol

Bruyette: Let's discuss testing now. What is the definitive test for diagnosing Addison's disease? Discuss the testing protocol and some of the problems we're facing with Cortrosyn.

Kintzer: The definitive test for diagnosing Addison's disease is the ACTH stimulation test. The classic finding is very low to undetectable cortisol levels before and after the administration of ACTH. In most Addisonian dogs, the post-ACTH cortisol concentration is less than 1 µg/dl. I use Cortrosyn intravenously at 5 µg/kg. I draw a pre-ACTH blood sample and another sample one hour after administration. With this protocol, we're able to get multiple doses out of the vial of Cortrosyn. We refrigerate it for up to four weeks and find that it maintains its potency. The current issue with Cortrosyn is that the marketing rights have been purchased by another company and the cost has increased. We were paying about \$150 for a box of 10 vials; the new price is about \$700 per box.

Behrend: The old protocol was to give one vial per dog. I think a lot of clinicians are still using

Points to Consider

- Often these patients have seen their veterinarian recently for nonspecific gastrointestinal signs, and they were treated with fluids and an injection.
- Dogs can also present with clinical signs and laboratory abnormalities suggestive of acute renal failure.
- The definitive test for diagnosing Addison's disease is the ACTH stimulation test.
- Studies have shown that 5 µg/kg of Cortrosyn intravenously—up to a maximum of one vial per dog—is an adequate dose.
- Another reason we see Addison's cases referred is a diagnosis of acute renal failure.

Points to Consider

- Although some ACTH gels are available, they are not recommended because the results may not be accurate.
- Prednisone, prednisolone, and hydrocortisone cross-react with cortisol and should be avoided for 12 hours before an ACTH stimulation.
- Practitioners should perform an ACTH stimulation test and not make a diagnosis based on electrolyte abnormalities and clinical presentation alone.
- Endogenous ACTH determination is better than aldosterone determination for differentiating primary and secondary disease.

that approach. But a number of studies have shown that 5 µg/kg intravenously—up to a maximum of one vial per dog—is an adequate dose. It's much less costly. Split any leftover, reconstituted Cortrosyn into aliquots using plastic syringes. For a vial of 250 µg, split it into five aliquots of 50 µg each or 10 aliquots of 25 µg each. For a 10-kg dog, use a 50 µg syringe. For a 5-kg dog, use a 25 µg syringe. You can freeze the aliquots for up to six months with no loss of activity as long as they're not thawed and refrozen. Because no one really knows the effects of thawing and refreezing ACTH, we don't recommend it.

Scott-Moncrieff: We are still using the one vial per dog protocol. My understanding is that it can be given either intravenously or intramuscularly, although we give it intramuscularly. We plan to start using the 5 µg/kg dose. I have hesitated to modify the dose because the studies evaluating the lower dosage involved normal dogs and dogs with Cushing's disease but not dogs with Addison's disease. Can we be sure that we're maximally stimulating the small vestiges of some of these dogs' adrenal glands? Chances are that the 5 µg/kg dose is just fine. I would be interested in everyone else's clinical experience regarding this protocol.

Bruyette: I think it's effective. I was at a human endocrine meeting recently where they were advocating a 1 µg per person dose to detect subclinical hypoadrenocorticism. So even 5 µg/kg may be a superphysiologic dose. I'd be surprised if you could detect Addison's disease in dogs using the whole bottle that you would miss using the 5 µg/kg dose.

Kintzer: Is the ACTH gel available again?

Greco: Some gels are available, but I don't recommend using them because the results may not be accurate.

Bruyette: I agree. We've all had too many problems with gel preparations. We need to stick with Cortrosyn for better or worse and to look at lower dosing and more conservative use. Are there any other points about ACTH stimulation that we should stress for practitioners?

Behrend: Before you do an ACTH stimulation test, remember that prednisone, prednisolone, and hydrocortisone cross-react with cortisol. Those drugs need to be avoided for 12 hours before you do an ACTH stimulation. Dexamethasone doesn't cross-react, but practitioners often ask me if it will

affect the results in another way. Will it suppress the adrenal gland? After one dose of dexamethasone, you may see a small suppression, but the results won't look like an Addisonian. If the post-ACTH cortisol concentration is just under the normal range, you're probably seeing the effect of the dose of dexamethasone. But if the serum cortisol concentration is zero pre- and post-ACTH, the dog has Addison's disease.

Scott-Moncrieff: I agree. I also want to stress how important it is that the practitioner perform an ACTH stimulation test and not make a diagnosis based on electrolyte abnormalities and clinical presentation alone. One of the most frustrating problems I encounter involves practitioners who've made a clinical diagnosis of Addison's disease without confirming it with an ACTH stimulation test. A few weeks later, they want to know how to confirm the diagnosis because the owners are finding treatment expensive. The problem is that the animals are now on Percorten-V, Florinef, or prednisone. You need to withdraw those drugs for a fairly long period of time to interpret the ACTH stimulation test. If the dog does have Addison's disease, it can have an Addisonian crisis during that time. It really pays to get your diagnosis up front. It's very difficult to confirm the diagnosis retrospectively.

Kintzer: And if an animal with an ACTH stimulation result consistent with Addison's disease has normal electrolyte concentrations, we should encourage practitioners to measure endogenous ACTH or aldosterone concentrations to differentiate primary from secondary hypoadrenocorticism. If it's a secondary case (pituitary ACTH deficiency), it's less expensive to treat.

Scott-Moncrieff: And you don't have to spend as much money monitoring monthly electrolyte concentrations.

Behrend: I agree. Endogenous ACTH determination is better than aldosterone determination. Then you know for sure whether it's primary or secondary Addison's disease. If the aldosterone concentrations are normal initially, that doesn't mean they won't become abnormal later. With primary Addison's disease, endogenous ACTH will be greatly elevated; with secondary disease, endogenous ACTH is very low or nondetectable. A dog that has normal electrolytes at presentation but has primary Addison's disease often develops electrolyte abnormalities in the future. A dog with

secondary Addison's will never develop electrolyte abnormalities. Measuring aldosterone does not give you the same information as endogenous ACTH. If the aldosterone is normal when measured, you still don't know if the dog has primary or secondary Addison's, so you don't know if it is possible for electrolyte abnormalities to develop.

Potassium and sodium concentrations

Bruyette: Let's move on to the next question which we've touched on already. Why do some Addisonian patients have normal potassium and sodium concentrations?

Behrend: I'm not sure I have a good answer. The easy answer is that those Addisonian patients are not mineralocorticoid-deficient. Either they will never be (if they have secondary Addison's disease) or they're not to that point (if they have the primary disease). For patients that do have low aldosterone concentrations, it's possible for one electrolyte concentration to be abnormal but not the other. Other factors can affect sodium and potassium concentrations such as dehydration. For example, a sodium concentration that would have been low looks higher because the animal is dehydrated. But, in aldosterone-deficient animals, if either electrolyte concentration is normal when you first test them, it may become abnormal if you retest them within a few days.

Bruyette: I've certainly seen that occur—especially in dogs with a lot of vomiting and diarrhea. Their electrolytes are not typical for Addisonians. But then they're rehydrated and the potassium concentrations increase and the sodium concentrations decrease.

Scott-Moncrieff: But conversely, sometimes we see animals that have a more classic Addisonian electrolyte presentation initially, then other factors come into play and their potassium concentrations normalize. I think the important point is not to rely on electrolytes as the only diagnostic test.

Greco: I agree. We also need to keep in mind that conditions other than Addison's disease can cause this abnormal ratio, too. High potassium and low sodium concentrations can be seen with whipworms. The bottom line: Don't skip the ACTH stimulation test.

Treatment

Bruyette: Why don't we move on to treatment

options? The question is a broad one. What are the treatment options for Addison's disease? I guess we can divide it into primary vs. secondary disease.

Greco: Mineralocorticoid replacement is the most common treatment since primary Addison's disease occurs more frequently. We have two options: Florinef and Percorten-V. Each drug has advantages and disadvantages—Florinef has both mineralocorticoid and glucocorticoid activity, and Percorten-V has mineralocorticoid activity. I tell clients that I prefer the injectable Percorten-V because I know the dog will get it for roughly 30 days. If it's a large dog, it tends to be less expensive than Florinef. The advantage of Florinef is that additional glucocorticoid therapy may not be needed, though in some patients it is. If you have an atypical Addisonian dog with normal electrolyte concentrations, only glucocorticoids are required, and glucocorticoids are much less expensive than either Florinef or Percorten-V. Of course, in the patient with electrolyte abnormalities, mineralocorticoid replacement is needed.

Bruyette: The primary complaint we get from clients whose pets are being treated for Addison's disease is polyuria and polydipsia. I would like the group to discuss whether the cause is the prednisone, the mineralocorticoid, or both. How do you approach the patient that is PU-PD?

Greco: Those are the hardest to deal with. If they're on Florinef, I switch them to Percorten-V and use a very low dose of prednisone—the smallest dose I can possibly give.

Behrend: What's the lowest dose you use?

Greco: I might use 1 mg for a 100-lb dog.

Scott-Moncrieff: I see much more PU-PD in dogs treated with Florinef than in dogs treated with Percorten-V. But I've seen it with both. I will often give prednisone and taper it based on clinical findings. With a 100-lb dog, I may give 2.5 mg of prednisone—or even less—every second or third day. That seems to be enough. I start with a standard dose so the owner knows how good the dog can feel, and then I use the owner's intuition about the pet's needs for glucocorticoid supplementation.

Greco: I agree, but I want to make one other point. Many times these clients aren't complaining about PU-PD. They're complaining about incontinence due to estrogen deficiency. I'm

Points to Consider

- It's important not to rely on electrolyte concentrations as the only diagnostic tests for Addison's disease.
- Think Addison's disease in dogs presenting with nonspecific signs of gastrointestinal disease.
- I see more PU-PD in dogs treated with Florinef than in dogs treated with Percorten-V.
- For the patient who is PU-PD, I switch to Percorten-V and use the smallest dose of prednisone I can possibly give.

Points to Consider

- With Percorten-V, I start at 2 mg/kg and taper that dose over time, giving it once every 30 days. If the patient does well, I decrease the next dose by 10 percent.
- I have dogs with normal electrolyte concentrations on as little as 1 mg/kg of Percorten-V per month.
- It's usually preferable to have owners bring their dogs in for the injections, rather than administering them at home.
- When I start Percorten-V, I check electrolytes before each dose while I'm tapering the dose.

especially suspicious of this in dogs on Percorten-V and such a low dose of prednisone that I can't believe the prednisone is responsible. I give these dogs diethylstilbestrol on a weekly basis.

Bruyette: Their urine specific gravities aren't low?

Greco: Correct.

Kintzer: You could ask clients to measure water consumption. I've treated dogs with Florinef and no prednisone that were PU-PD; when I switched to Percorten-V, it resolved because Florinef can cause PU-PD.

Bruyette: I agree. All of us have seen more PU-PD with Florinef than with Percorten-V, although it does occur. And it's interesting that we're talking about using replacement doses of prednisone well below the 0.25 mg/kg daily dose that's considered physiologic. Patients who take that amount of prednisone on a daily basis may become polyuric and polydipsic.

Behrend: With Florinef, about half the dogs are on prednisone and half are not. With Percorten-V, it worries me to not have them on daily doses of prednisone. It may be a very low dose, but Percorten-V has no glucocorticoid action. They're basically glucocorticoid-deficient on the days you do not give them prednisone. I don't know if that causes any problems—I don't think anyone has studied it.

Greco: I agree. Most of my patients on Percorten-V are on daily prednisone, though I've had a few dogs on prednisone every other day.

Kintzer: One point to add is that in times of stress—such as hospitalization or trauma—the prednisone dose should be increased.

Scott-Moncrieff: I don't worry about animals that are given prednisone every other day, or every third day, if they're doing well clinically. Animals usually don't have an acute crisis due to glucocorticoid deficiency. If they're going to develop glucocorticoid deficiency, you get lots of warning. I only extend the prednisone dosage frequency in animals that are having problems with PU-PD. Typically, these animals feel better when they're getting lower doses of glucocorticoids. I'm guided by owners' reports of how the dogs are doing.

The other point I want to make is about dosing these drugs. With Florinef, I start with 0.02 mg/kg, but I have to increase that dose signifi-

cantly to keep electrolyte concentrations normal. Whereas, my experience with Percorten-V is that I start at 2 mg/kg and taper that dose over time, giving it once every 30 days. If the patient is doing well clinically, I'll decrease the next dose by about 10 percent. I find dogs can maintain normal electrolyte concentrations on as little as 1 mg/kg of Percorten-V per month. That can make a huge difference in the expense for a large dog.

Greco: I do the opposite. I increase the interval. I've treated 150-pound dogs with Percorten-V—the drug would normally be cost-prohibitive, but I was able to extend the interval to 50 days. The price was cut in half. You do have to monitor them closely, though.

Scott-Moncrieff: My two concerns about doing that are whether the owners will remember the treatment and how you can monitor the patients in the meantime. If you get them on a once-a-month schedule, you get to monitor them every month and the owners can mark it on their calendars to get a Percorten-V injection. A monthly schedule is more practical for the owners. But I agree it will work either way.

Kintzer: I also want the patients in once a month. It's easier for everyone to remember.

Drug administration

Bruyette: Here are some other common questions I get from practitioners. Can I give Percorten-V subcutaneously? Can I let the owners administer it at home? How many of you are using it subcutaneously and how many of you let clients administer the medication at home?

Kintzer: I administer it subcutaneously.

Greco: I do, too.

Behrend: I don't let owners administer it, though.

Bruyette: Are you concerned about owners improperly administering the medication?

Kintzer: In a diabetic, if the owners miss a dose of insulin or administer it improperly, it's not that big of a deal since injections are given twice daily. But with Percorten-V, not only is it more expensive, but you're not sure how much the patient got and how long it will last.

Scott-Moncrieff: I typically have owners bring

the pet in and we administer it. But if an owner was eager to administer the drug at home and I thought he or she was capable, I'd probably allow it.

Greco: It's also a question of whether or not they can afford it. If you can save them an office visit, the cost of treating the dog decreases.

Kintzer: In that case, I'd have a nurse do it.

Scott-Moncrieff: When I start Percorten-V treatment, I check electrolytes before each dose while I'm tapering the dose. Once I determine the lowest effective dose, I check electrolytes every three months. At that point, it would be reasonable to let the owner or a technician administer the drug.

Treatment intervals

Bruyette: Based on your experience, how long does it take to get patients stabilized on their medications so that they're asymptomatic, feeling well, and have normal electrolyte concentrations? One of the concerns about Addison's disease is that it's an expensive disease to treat. Hopefully, these dogs are going to live a long time and they will be on long-term medication. The early stages of treatment will be much more expensive than the follow-up period. How long do you tell clients it will take before you have the right dose and dosing interval?

Scott-Moncrieff: If the owners want to taper the Percorten-V dose, it takes four to six months to find the minimum effective dose. It costs more initially because you're monitoring electrolyte concentrations, but less in the long run because you're administering less of the drug.

Kintzer: I'd check the electrolytes three and four weeks after the first dose so I know how long the drug is lasting.

Scott-Moncrieff: We do that, too, because the label duration is 25 days. We usually check patients at 21 days and if they're looking good, we try to extend them to a 30-day interval.

Behrend: In my experience, Florinef is more difficult to regulate at the beginning of treatment. You're checking electrolytes much more often until you settle on the dose. Sometimes the optimum dose changes over time during the first year for whatever reason. With Percorten-V, I've learned that once I find the dose, I don't have to change it much.

Bruyette: One other problem with Florinef is that you'll find a dose where the potassium concentration is fine, but the sodium concentration is still low. If you increase the Florinef dose to increase the sodium concentration, then it's much more expensive. The electrolyte concentrations are fixed more readily with Percorten-V than with Florinef.

Scott-Moncrieff: I'd agree. We used to worry about hyponatremia with Florinef. With Percorten-V, that just isn't an issue. When we've switched dogs from Florinef to Percorten-V, their electrolyte concentrations have dramatically improved and they've felt better. I suspect that dogs on Florinef with hyponatremia are underdosed. I don't think dogs absorb Florinef as well as Percorten-V.

Before we leave the treatment issue, should we address the topic of what to do with an Addisonian animal that's not responding appropriately to therapy? Occasionally, we'll treat an animal, it stabilizes, and its electrolytes stabilize, but it just doesn't act normal. We see this more often with Florinef than with Percorten-V.

First, you should look at their replacement therapy dosage to make sure they're being appropriately dosed. Look at the prednisone dose and make sure that it's adequate—not too high. Then also consider that these animals can have concurrent diseases. These dogs might have endocrinopathies such as hypothyroidism as well as other conditions like inflammatory liver disease or gastrointestinal disease.

Kintzer: If they're on Florinef, you might switch them to Percorten-V.

Scott-Moncrieff: Absolutely. That would be my first line of therapy, especially if their electrolytes are outside the reference range.

Greco: But I no longer salt the food.

Scott-Moncrieff: No.

Bruyette: Many of these dogs are young and are going to live for a number of years. One of the problems that practitioners encounter is that every time these patients aren't feeling well, they immediately assume it's the Addison's disease. But several other problems can surface over time that will make these dogs sick or make treatment for Addison's disease less effective.

Kintzer: And if they're sick from something else, they may need more prednisone than they're

Points to Consider

- When we've switched dogs from Florinef to Percorten-V, their electrolyte concentrations have dramatically improved and they've felt better.
- We usually check patients at 21 days and if they're looking good, we try to extend them to a 30-day interval.
- In my experience, Florinef is more difficult to regulate at the beginning of treatment. With Percorten-V, I've learned that once I find the dose, I don't have to change it much.
- The electrolyte concentrations are fixed more readily with Percorten-V than with Florinef.

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Points to Consider

- If you say you're not seeing Addison's disease, I say Addisonians are seeing you.
- Addison's disease is easily treatable and dogs do great, but owners should never forget that this is a deadly disease.
- If dogs make it through the Addisonian crisis and are treated appropriately, they die of other conditions but not Addison's disease.
- Treating a dog with Addison's disease is the ultimate practice builder. The clients are always grateful; you'll have a client for life.

getting for Addison's disease.

Scott-Moncrieff: In the older animal with Addison's disease, there may be an underlying cause for its disease such as lymphoma in the adrenal glands or other neoplastic involvement.

Precautions for Addison's patients

Bruyette: A common scenario is that you have a well-regulated Addisonian patient who now needs to undergo general anesthesia for an elective procedure. How much would you increase the dose of prednisone for that procedure and for how long?

Behrend: That's a hard question. The literature states anywhere from two to 10 times the current dose. I use that as a guideline and try to estimate how serious the stress is such as boarding vs. major surgery. I'd rather overdose patients for a few days than underdose them. I tend to start high and then taper the dose relatively quickly after the stress is over. If it's a major elective procedure, such as surgery with general anesthesia, go high for a couple of days and then taper off quickly. When the patient goes home, keep it a bit above the normal dosage for another week and then go back to the normal dose.

Bruyette: For elective procedures involving general anesthesia, the most important thing you can do is to provide fluid support during the anesthetic episode. Most of the studies in adrenalectomized rats suggest that even without glucocorticoids, the patients do fine in terms of blood pressure as long as they're getting fluids. It's the animals that are not being fluid-loaded during the procedure that may have problems.

Greco: Unless the patients can't be fluid-loaded, such as dogs with heart problems.

Behrend: Another option for stressful procedures such as surgery is to give dexamethasone during the surgery. Oral steroids will still need to be given postoperatively.

Conclusions

Bruyette: The last question is a global one. What take-home points would you like to leave practitioners with regarding Addison's disease?

Behrend: Addison's disease can look like a lot of different conditions. You need to keep it on your

rule-out list even if the classic electrolyte abnormalities aren't present or if only one of the two electrolyte changes is present. And you need to get a definitive diagnosis.

Scott-Moncrieff: I'd emphasize that whenever you're working up an animal with systemic illness, you should ask yourself if it could be Addison's disease. At least have conditions of the adrenal gland on your differential diagnosis list. If you ask yourself the question, then you'll increase your index of suspicion and not miss the diagnosis.

Greco: If you say that you're not seeing Addison's disease, I say Addisonians are seeing you.

Kintzer: The take-home point is to maintain a high index of suspicion because you're not going to find Addison's disease if you aren't looking for it.

Behrend: Also, I'd stress that client communication is important—I stress to clients that Addison's disease is easily treatable and the dogs do great, but they shouldn't forget that it's a deadly disease. Missing a dose of a medication is a big deal, especially if they're on Florinef. Just skipping the pill for a day—"Oh, I'm going out of town and it's a hassle to have someone come over to pill the dog"—is not an option.

Bruyette: That's a very good point. It's much different than simply missing a dose of insulin.

Behrend: If you miss a dose or two of Florinef, it could be fatal.

Kintzer: Following a study of 205 dogs treated for Addison's disease, I called clients years later and invariably, they were satisfied with how well their pets did. We didn't find dogs that died of Addison's disease—If they made it through the crisis and were treated appropriately, they died of conditions other than Addison's disease.

Greco: It's the ultimate practice builder. The clients are always grateful; you'll have a client for life.

Bruyette: Thank you all for a very helpful discussion on Addison's disease. It's clear we still have many questions to answer regarding this increasingly common endocrine disease. Hopefully, we've addressed some of the more common questions we as practitioners face every day.