

Low Dose Percorten Information – Please share with your vet

CVC 2008 Highlights: Managing atypical and critical cases of primary hypoadrenocorticism in dogs – David S. Bruyette, DVM, DACVIM

from: <http://veterinarymedicine.dvm360.com/cvc-2008-highlights-managing-atypical-and-critical-cases-primary-hypoadrenocorticism-dogs>

“Furthermore, I have found that large dogs (> 50 lb) may need only 0.5 mg/lb DOCP, and if their electrolyte concentrations are normal at four weeks after the first injection, you may be able to effectively treat these patients with an even lower dose. DOCP is also effective when given subcutaneously,⁶ and we have taught our clients how to administer these injections at home, thus saving the expense and time of a trip to the hospital for dogs that are stable.”

Dr. Julia Bates - The following two articles are included in their entirety below. The original documents may be found at the following links:

Lower initial dose desoxycorticosterone pivalate for treatment of canine primary hypoadrenocorticism - Julia A. Bates, DVM, DACVIM (SAIM)

<http://onlinelibrary.wiley.com/doi/10.1111/avj.12019/abstract>

Link for Interview with Dr. Julia A. Bates:

http://www.addisondogs.com/addisons/articles/julia_bates_interview_2012.pdf

Lower initial dose desoxycorticosterone pivalate for treatment of canine primary hypoadrenocorticism - Julia A. Bates, DVM, DACVIM (SAIM)
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SMALL ANIMALS

Lower initial dose desoxycorticosterone pivalate for treatment of canine primary hypoadrenocorticism

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Keywords:

companion animal medicine; dogs; endocrinology; hypoadrenocorticism

Objective

To evaluate the efficacy of initial doses of desoxycorticosterone pivalate (DOCP) that are lower and less expensive than the presently recommended initial dose of 2.2 mg/kg for treating dogs with primary hypoadrenocorticism.

Methods

A retrospective study was performed on 49 dogs with primary hypoadrenocorticism, including 36 with initial DOCP doses less than 2.2 mg/kg. Medical records were reviewed for clinical data. All study dogs were followed up with telephone calls to owners or veterinarians to determine the date of death or last follow-up. Data were analysed to investigate relationships between initial DOCP dose and survival and serum Na, K and their ratio.

Results

Regardless of their initial DOCP dose, none of the dogs developed uncontrolled hypoadrenocorticism or severe electrolyte abnormalities or clinical problems that would have made an increase in the DOCP dose necessary. Over time, most dogs had a decrease in their DOCP dose in mg/kg, because of weight gain during treatment. No statistically significant relationships were found between initial DOCP dose and survival or post-treatment serum Na, K or Na : K, with the exception of one statistically significant result that suggested lower efficacy for higher doses.

Conclusion

Initial DOCP doses less than 2.2 mg/kg may be effective in controlling serum electrolyte concentrations in dogs with primary hypoadrenocorticism without adversely affecting survival. If confirmed by additional research, these findings would enable practitioners to reduce the cost of DOCP treatment by using lower initial doses, potentially saving the lives of dogs that would otherwise be euthanased because of treatment expense.

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Addison Dogs Interview

With Dr. Julia A. Bates, DVM, DACVIM

Julia A. Bates, DVM, DACVIM currently practices veterinary medicine at Madison Veterinary Specialists in Madison, Wisconsin. She is an internal medicine specialist with strong interests in cardiopulmonary, immune mediated and endocrine diseases. Her clinical research interest is in hypoadrenocorticism (Addison's disease). Dr. Bates et al. recently had a retrospective study, "Lower Initial Dose Desoxycorticosterone Pivalate for Treatment of Canine Primary Hypoadrenocorticism," accepted for publication in the *Australian Veterinary Journal*.

Dr. Bates, you seem to have a special interest in Canine Addison's. What led to this interest?

As internists, we deal with a large number of cases with poor prognoses and we are often giving bad news to owners. In the case of Addison's disease, it is one of the few times that we get to be the hero. Dogs diagnosed with Addison's disease should have a very normal life with a very normal lifespan.

The Novartis Percorten-V insert states to begin treatment with Percorten at a dose of 1.0 mg/lb every 25 days. That is not how you begin Percorten treatment. Can you explain how you decide on the appropriate starting dose?

I spent three years at Michigan State University doing a residency in Small Animal Internal Medicine, where we are trained to use a lower starting dose. Prior to the FDA approval of DOCP, dogs diagnosed with typical hypoadrenocorticism (Addison's disease) at MSU were typically treated with 1 mL (25 mg) per dog per month. As residents, sometimes we would be nervous about that low of a starting dose, especially in a very large breed dog and may have given a higher dose such as 2 mL (50 mg) per dog.

Retrospectively, I looked at many dogs treated with a low starting dose and only one dog required a dose increase (it was a young lab that had recurring UTIs). The other dogs did great. Several dogs received and did well on a dose of 0.3 mg/kg (0.14 mg/lb).

When I initially start treatment the dose I start with is variable, but typically somewhere in the range of 25 mg - 50 mg total dose per dog. If I am speaking with a family veterinarian, I recommend starting at a dose no higher than 1 mg/kg (0.45 mg/lb).

Is the dose range you use for small breeds any different?

I would feel very comfortable with a starting a small dog on 1 mg/kg (.45 mg/lb).

Once you start a dog on Percorten, how do you monitor the dose and how do you decide if the dose needs to be reduced or increased?

I follow general accepted treatment guidelines of checking electrolytes on day 12 and 25 following administration of DOCP. If the electrolytes are abnormal on day 12, then the dose should be increased. Day 25

electrolytes and after are used to determine the interval in between injections. In my experience, most dogs do well on a 28-30 day interval. It seems that many dogs will initially have a longer duration of the first injection, but over time, it decreases to approximately every 30 days.

When a dog requires a decrease in Percorten, how do you determine the amount of the decrease? For example, Novartis recommends no more than a 10% decrease at any one time. Because I typically start with such a low dose, it is uncommon for me to decrease it; however, a 10% reduction is reasonable.

If a dog's potassium is rising but not out of normal range, at what point would you decide to increase the Percorten?

I am a big believer of treating the patient and not a number, so it depends on how the dog is doing and how the numbers are trending.

The Novartis Percorten insert states that Percorten must be given IM but many of our list members give it SQ. Do you recommend giving Percorten SQ or IM and why?

McCabe MD, Feldman EC, Lynn RC,

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et al. Subcutaneous administration of desoxycorticosterone pivalate for the treatment of canine hypoadrenocorticism. *Journal of the American Animal Hospital Association* 1995; 31:151-155. This paper looked at using SQ dosing of DOCP in 12 dogs, both newly diagnosed and ones previously receiving IM injections. All dogs maintained normal electrolytes supporting the use of SQ injections.

If a dog is not well hydrated, or I am concerned about SQ absorption, I will often give the first injection IM, followed by SQ injections. That being said, there are dogs that may do better with IM injections rather than SQ, especially if they are overweight. Personally, I am a firm believer of treating the patient rather than sticking to dogma.

Do you think it is appropriate for pet guardians to be taught to give Percorten injections to their own dogs?

Most definitely! Personally, I believe owners play a big role in the management of dogs with Addison's disease. Subtle changes in a dog's behavior can often be an indicator of abnormal electrolytes. I also encourage owners not to be afraid of varying the dose of Prednisone without consult. It is important to know the signs of too much and too little corticosteroids; that being said, it is often much easier to recognize too much Prednisone rather than too little. Unless of course the dog has developed GI signs (vomiting, diarrhea, etc.).

Why do you think there is the persistent misconception in the veterinary community that dogs with Addison's disease only need Percorten and not Prednisone with Percorten? There seems to be confusion about that issue.

I don't know if I would call it a misconception; although there are many people involved in this group, Addison's disease is not that common, and so most family veterinarians will only see a few cases in their entire career. Family veterinarians treat multiple species and are both diagnosticians and surgeons. Therefore, it is difficult to know the intricacies of all diseases.

As an internist, I only see cases with medical problems; I don't treat skin issues, perform surgery or administer vaccinations. This is why it is important to be aware that there are veterinary specialists who may be able to help your pet and your veterinarian, in the diagnosis and management of complex disease processes.

We tend to see veterinarians dose Percorten at 1mg/lb. (2.2 mg/kg) and never change that dosing method regardless of how low the potassium is at day 25-28. What would you say to these veterinarians to get them to use low-dose Percorten?

I can't say anything to them, other than to share my personal experience in treating many of these dogs. Unfortunately, there is no published literature in the routine use of low-dose DOCP to treat dogs with Addison's disease.

It is reasonable to want evidence supporting a change of the status quo, especially given the cost of treatment and risk associated with an Addisonian crisis. My personal experience combined with that of my mentors makes me feel comfortable using DOCP in an off label manner. It is also important to understand the veterinarians are responsible for consequences when using a drug in an off label manner. I think pet owners

don't realize the cost of our license to practice veterinary medicine: four years of undergraduate education, four years of veterinary school and for me, one year of an internship, three years of a residency, two exams and a publication. Not to mention the cost of education. Many of us have six-figure student loan debt. So, as you may be able to imagine, there isn't much that is worth doing to lose your license.

How many dogs with Atypical Addison's do you see/diagnose compared to Typical's? How many Atypical's transition to Typical's?

That's a difficult question to answer, as many "typical" cases are diagnosed by emergency clinics and family veterinarians are recognizing it more than in the past. Therefore, I would say I see more atypical cases. Transition also varies, but I would say most dogs that are atypical stay atypical. In my opinion there is a small population of dogs that are diagnosed very early and have normal electrolytes, so it appears that they go on to transition to "typical" Addisonians. That could vary among practitioners.

Do dogs with Atypical Addison's need Percorten?

No! Dogs with atypical Addison's disease have a glucocorticoid deficiency, meaning that they don't have enough circulating cortisol, the stress hormone, to deal with physiologic stress or in some cases to maintain life. These dogs only require replacement of prednisone. These dogs have NORMAL electrolytes. Dogs with typical Addison's disease lack both glucocorticoids and mineralocorticoids. Mineralocorticoids are important for maintenance of water balance and sodium and potassium. DOCP (Percorten) is a mineralocor-

ticoid replacement hormone and is not needed in patients that are only glucocorticoid deficient. There is also a small subset of dogs that may be only mineralocorticoid deficient, requiring DOCP, but not Prednisone.

In the long term, are there any health risks associated with a dog receiving more Percorten than they need?

Not that I am aware of. There have been several studies looking for evidence of hypertension in dogs treated with high doses of DOCP, yet no serious side effects have been identified.

Anecdotally, there are many reports of dogs receiving published doses (2.2 mg/kg or 1 mg/lb) of DOCP showing signs of aggression, increased thirst, increased urination and appetite. Decreasing the dose has led to resolution of the signs.

What are the risks of potassium that goes too low from over treatment with Percorten?

There are no published accounts of dogs suffering from hypokalemia (low potassium) secondary to DOCP injections. However, hypokalemia can lead to severe muscle weakness.

Have you ever seen a dog that did not respond to treatment with low-dose Percorten?

No

Some sources say to dose Percorten once every 25-28 days, others say 30-35 days, which do you recommend?

Dosing interval of DOCP is based on electrolytes. Most literature states that most dogs require a dosing in-

terval of every 21-25 days. In my experience it is typically every 28-30 days. There are those (Dr. Deb Greco — one of my mentors during my internship), who advocate giving a higher dose of DOCP to increase the interval between injections. In my experience, I have seen dogs not require their next dose of DOCP for up to 60 days following the initial injection. However, most of those dogs leveled out over time to every 30 days.

What is the lowest, average and highest dose of mg/lb of Percorten you have used?

I don't typically treat on a mg/kg basis. I treat per dog usually somewhere between a total dose of somewhere between 25 mg and 50 mg per dog, for large dogs.

How effective is a resting cortisol to rule out Addison's if a pet guardian cannot afford the ACTH test?

Great question! Yes, a baseline or resting cortisol of >2.0 ug/dL in a dog not on medications that affect adrenal function makes the diagnosis of Hypoadrenocorticism very unlikely. However, if the baseline cortisol is <2.0 ug/dL an ACTH stimulation test needs to be performed to rule Addison's disease in or out. It is important to know that a baseline cortisol measurement CANNOT be used to confirm the diagnosis of Addison's disease.

[*Journal of the American Veterinary Medical Association*
August 1, 2007, Vol. 231, No. 3, Pages 413-416

doi: 10.2460/javma.231.3.413
Use of basal serum or plasma cortisol concentrations to rule out a diagnosis of Hypoadrenocorticism in dogs: 123 cases (2000–2005) Elizabeth M. Lennon, BS; et al]

When and how should you use the endogenous ACTH concentrations?

Endogenous ACTH concentrations can help you determine if the Addison's disease is primary (destruction of the adrenal glands) or secondary (lack of ACTH). It is more academic than clinically relevant, as it won't change how one manages the disease. Clinically, it can be more helpful in localizing the diagnosis of Cushing's disease (hyperadrenocorticism). The ACTH hormone is very labile, and proper handling is required to ensure valid results.

What dose of Cortrosyn do you use for the ACTH test?

5 ug/kg IV; I don't use or advocate the use of the ACTH gel, as it can lead to questionable results.

Is there ever any need to use the ACTH test as a monitoring tool once a dog has been properly diagnosed with naturally occurring Addison's or is it ever appropriate to use the ACTH test to determine the Prednisone dose?

No, never. If a dog develops Addison's secondary to treatment for Cushing's disease, follow up ACTH stimulation tests may be needed to determine if the adrenal glands have recovered.

If a pet guardian is refusing the ACTH test and you believe based on clinical signs and initial blood work that their

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If I am speaking with a family veterinarian, I recommend starting at a dose no higher than 1 mg/kg (0.45 mg/lb).

Although there are published doses of physiologic Prednisone (how much the body needs to survive), in my opinion that amount varies from dog to dog. Many dogs do well on a much lower dose of Prednisone than what is published.

dog has Addison's, can you use Percorten safely?

Why would you? Although the cost of an ACTH stimulation test can be expensive, an appropriate diagnosis will save time and money in the long run. It is unlikely that I would just empirically treat a dog for Addison's disease without supporting ACTH stimulation test results.

What is the best resource a veterinarian can have on hand for diagnosing and treating Addison's?

Feldman & Nelson's book, *Canine and Feline Endocrinology and Reproduction*, and the telephone number of an internal medicine specialist.

Is in-house monitoring equipment adequate for checking electrolytes, or do you prefer a reference lab?

Yes. However, that being said, any time I receive what I suspect is an aberrant result, I recheck the result with a veterinary reference lab.

If a dog with Addison's disease has signs of early kidney disease, is it still safe to use Percorten?

Yes! There is no disease process that I am aware of (other than an aldosterone secreting tumor) that would preclude the use of DOCP in a dog with typical Addison's disease.

How important is Prednisone or a similar steroid in the treatment of Canine Addison's?

It is very important ... unless it is the very rare case of just being mineralocorticoid deficient. Every cell in the body requires corticosteroids to function normally. Without it, you will die.

How do you decide on what dose of Prednisone a dog requires?

The amount of Prednisone a dog requires varies by dog and the amount of physiologic & physical stress they are under. It also depends if they are in the middle of a crisis or have been recently diagnosed.

Typically, I initially treat newly diagnosed dogs with a higher dose until they develop signs of excess cortisol (increased, thirst, urination, panting, etc.), then have the owners gradually decrease the dose until the signs resolve. The most difficult part is attempting to determine the absolute lowest dose each patient requires. In my opinion, I like patients to have a very normal life, with no side effects from the Prednisone. If they seem off, yet their electrolytes are normal, I will likely have owners increase the Prednisone dose.

Personally, as I've mentioned previously, I really like owners to feel empowered to adjust the dose of Prednisone based on how their pet is doing. If it is an active hunting dog, it may require more during hunting season, and less other times of the year.

What is the lowest, highest and average dose (mg/lb/kg) of Prednisone you have used?

It varies on the patient. One dose doesn't fit all dogs. Dogs in the midst of a crisis or under stress require higher amounts.

Prednisone is documented to have some minor mineralocorticoid activity. At what dose mg/lb would you have to give for it to have any effect on the electrolytes?

That's a good question, but I don't know the answer. However, I would suspect that it would have to be a high enough dose in which the patient would exhibit signs of cortisol excess (too much Prednisone).

What are the biggest or most common mistakes you see in the care of Addison's patients?

I don't know if I would use the word mistake, but there are many practitioners (in the U.S.) that do things differently than I would. I would say the most common is using Florinef rather than DOCP. All the literature, as well as my personal experience, supports that dogs with Addison's disease are typically better regulated on DOCP than on Florinef. Many also use a fixed dose of Prednisone, which personally I am not a fan of. Although there are published doses of physiologic Prednisone (how much the body needs to survive), in my opinion that amount varies from dog to dog. Many dogs do well on a much lower dose of Prednisone than what is published.

It has been suggested that dogs with Hypothyroidism (being treated with Soloxine) clear steroids faster from the body, so is it necessary to split the Prednisone dose and give it twice a day?

It would make sense that dogs being treated with thyroid replacement hormone will have an increased metabolism and potentially clear drugs faster. Unlike their human counterparts, absorption of thyroid replacement hormone from the GI tract of dogs is inefficient. This is why the dog dose is significantly higher than the human dose. Although a dog

Addison's disease is a very manageable disease. Dogs with Addison's disease should lead a normal life in every way other than requiring monthly injections and daily or every-other-day Prednisone.

receiving thyroid hormone replacement may clear steroids faster than a "normal" dog, my treatment strategy doesn't change. Although we have published physiologic dose ranges of Prednisone, the actual requirement can vary significantly from dog to dog. My personal philosophy is to educate owners to the signs of too much and too little Prednisone and to have a comfort level in changing the dose to find what works with their dog.

How do you recommend that Prednisone be reduced for dogs that have been on higher than needed doses for a long time?

Unfortunately, there is no one-size-fits-all answer. However, in most cases, I would likely recommend decreasing the dose by 25%-50%, depending on what clinical signs the dog was exhibiting. No matter how it's accomplished, as long as the Prednisone is not abruptly discontinued, the pet should not experience ill effects.

If a dog is currently taking a steroid other than Dexamethasone, how long should you wait once you stop the steroid to run the ACTH test?

It depends on the specifics of the case and how much corticosteroid was being administered, but likely somewhere in the vicinity of 3-7 days.

Is it possible for a dog who is on Prednisone for several weeks to several months to need more than one week to actually pass the ACTH test?

The longer a patient has been on Prednisone, the longer the results can be affected, resulting in misleading results. Results of an ACTH stimulation test can also be affected by how the test was completed and whether or not ACTH gel was used.

Should a CBC be run after the first month to make sure values are returning to normal? Please explain why/why not.

If values were abnormal to begin with, then yes, it is very reasonable to recheck to make sure things have normalized and we aren't missing some other underlying disease process.

Is there anything you would like pet guardians and veterinarians to know about Addison's?

Addison's disease is a very manageable disease. Dogs with Addison's disease should lead a normal life in every way other than requiring monthly injections and daily or every-other-day Prednisone.

Other than potentially hypothyroidism, dogs with Addison's disease have no greater risk of contracting other diseases than any other dog.

Most importantly, it is important not to panic. Most pet owners who have witnessed their dog survive an Addisonian crisis tend to live in fear. As long as your dog is being treated (especially with DOCP rather than Florinef), the likelihood of another crisis is almost non-existent.

Do you have any suggestions on how we can reach out to more vets, other than our own, on the latest and greatest about Addison's?

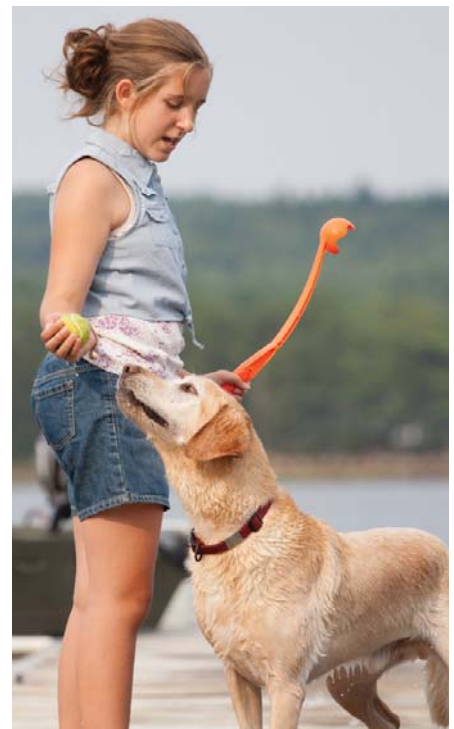
That's difficult to answer, other than sharing your experiences. It is also important to remember that if you feel that anyone in the medical profession isn't listening to you, then you should find another professional who will.

It can be especially important (and often cost-effective) to enlist the help

of a veterinary specialist early in the course of a disease. If your veterinarian doesn't offer referral, consider working with one who believes in the team approach to medicine.

Dr. Bates, on behalf of Addison Dogs, thank you so much for taking the time to answer our questions and helping to educate caretakers of Addison dogs.

Elizabeth Andrews is a moderator on the Addison Dogs online support group. She also is on the Board of Directors of her local animal shelter. She is owned by three Labrador retrievers, one of whom has Addison's disease. She is dedicated to helping others learn about the disease.



Elizabeth Andrews' granddaughter Aidan with A-Dog Raider who has been on low-dose per corten for several years now.