CASE STUDIES

Understanding Canine Addison's Disease

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Clinical signs

Hypoadrenocorticism (Addison's disease) results from failure of the adrenal glands to secrete glucocorticoids and mineralocorticoids. Most cases are due to primary adrenal failure, resulting in deficiency of usually both cortisol and aldosterone secretion from the adrenal cortex. Clinical signs may be vague, can wax and wane and include anorexia, vomiting, lethargy, depression, weakness, weight loss, diarrhea, shaking/shivering, polyuria, polydipsia, bradycardia, weak pulse and collapse. Owners may not realize how long their dog has been ill until treatment results in a dramatic improvement in activity level.

Laboratory abnormalities

Abnormalities on a complete blood count (CBC) may include anemia, eosinophilia, neutrophilia and lymphocytosis. Hemoconcentration and lack of a stress leukogram may also be present. A chemistry profile may reveal hyponatremia, hypochloremia, hyperkalemia, hypercalcemia and hyperphosphatemia. Not all dogs with hypoadrenocorticism have the expected electrolyte changes. Other biochemical abnormalities may include hypoalbuminemia, hypocholesterolemia, hypoglycemia and increased liver enzymes. Specific gravity of the urine is commonly less than 1.030. In dogs with hyperkalemia, abnormalities may be present on the electrocardiogram (ECG). These include a peaked T wave and shortening of the QT interval in mild hyperkalemia, widening of the QRS complex, decreased QRS amplitude, increased duration of the P wave, and increased P-R interval in moderate hyperkalemia, and loss of P waves and ventricular fibrillation or asystole in severe hyperkalemia. **Many other disorders may mimic the characteristic findings of Addison's disease.**

ACTH stimulation test

An ACTH (adrenocorticotropic hormone) stimulation test is necessary to confirm a diagnosis. Blood samples to measure serum cortisol levels should be collected prior to and one hour after injection of a synthetic form of ACTH (up to 5 µg/kg). To confirm the diagnosis both the pre- and post-ACTH cortisol concentrations should be less than the reference range for basal cortisol (2 µg/kg). Measurement of a basal cortisol of >2 µg/kg is a useful test to exclude a diagnosis of hypoadrenocorticism.

Treatment

Rapid initiation of treatment of confirmed Addison's disease is vital, especially if profound electrolyte abnormalities are present. Aims of treatment include correction of hypotension/hypovolemia, correction of electrolyte imbalances, provision of an immediate source of glucocorticoids, and correction of acidosis, hypoglycemia and hypercalcemia. Parameters that should be monitored during treatment include serum electrolytes and acid-base status, urine output, ECG and blood pressure. Fluid therapy and IV glucocorticoids should be continued until the animal is fully rehydrated and oral intake is possible.

The most appropriate treatment for long-term mineralocorticoid replacement is desoxycorticosterone pivalate (DOCP) at a starting dose of 2.2 mg/kg (1 mg/lb) every 25 days. The dose should be titrated to effect. In many cases the final individualized dose of DOCP is < 2.2 mg/kg. Prednisone is recommended for glucocorticoid replacement. The starting dose is 0.2 mg/kg per day and the dose should be tapered to the lowest dose that will control the clinical signs. It is important to avoid excess prednisone supplementation because this may result in manifestations of iatrogenic hyperadrenocorticism.

Case studies

The following case studies provide examples of the variable clinical signs of canine hypoadrenocorticism and the value of early diagnosis and prompt initiation of treatment with Percorten®-V (desoxycorticosterone pivalate injectable suspension). Percorten-V is indicated for the treatment of canine Addison's Disease.*

*For use as a replacement therapy for the mineralocorticoid deficit in dogs with primary adrenocortical insufficiency.

Important Safety Information

Do not use in pregnant dogs or in dogs suffering from congestive heart failure, severe renal disease, or edema. Reduce dosage in dogs showing signs of hypernatremia or hypokalemia. Like other adrenocortical hormones, Percorten-V may cause severe side effects if dosage is too high or prolonged. The most common adverse reactions reported were depression/lethargy, vomiting, anorexia, polydipsia, and polyuria. Some of these effects may resolve with adjustments in dose or interval of Percorten-V or concomitant glucocorticoid administration. See product insert for full product information.

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CASE IN BRIEF

Diagnosis and Treatment of Canine Addison's Disease

Signalment
9-year-old Male Neutered West Highland White Terrier

History
Owner reports an 8-month history of mild intermittent diarrhea that has become worse in the last two weeks. During this time the color of the feces has become very dark. The dog was receiving no medications apart from routine heartworm prophylaxis and sucralfate, which had been prescribed for suspected melena. The dog was last vaccinated ten months ago.

Physical examination
The dog was quiet but alert. Body temperature was normal at 101.5°F, heart rate was 80 beats per minute and respiratory rate was 20 breaths per minute. Body weight was 8.5 kg and body condition score was 4/9.

Diagnostic plan
Blood was collected for a CBC, serum chemistry profile and urinalysis. Abnormalities included hypoproteinemia, non-regenerative anemia, hypocholesterolemia and hypocalcemia (see tables 1 and 2). The urinalysis had a specific gravity of 1.025, with negative protein and a benign sediment.

Further diagnostic testing
Pre- and post-feeding bile acids were within the reference range. An ACTH stimulation test showed both a pre- and post-cortisol of < 1 µg/dl which was diagnostic for hypoadrenocorticism (Addison's disease). Endogenous ACTH concentration was elevated (813 pg/ml reference range 10-40) consistent with primary Addison's disease.

Initial treatment plan
Initial treatment was with prednisone 0.22 mg/kg PO q 24 hours. This dose was tapered to 0.1 mg/kg q 24 hours over the following month.

Monitoring and outcome
The dog was monitored carefully for signs of mineralocorticoid deficiency (polyuria, polydipsia, weakness, depression, bradycardia), and electrolytes were monitored monthly for the first three months and then every three months. Eight months later development of hyperkalemia and hyponatremia prompted treatment with Percorten-V (desoxycorticosterone pivalate injectable suspension) (2.2 mg/kg or 1 mg/lb IM q 25 days).

Veterinarian's comments
This case is a good example of atypical canine Addison's disease. If an ACTH stimulation test had not been performed in this dog, the Addison's disease would have been missed and the dog would have likely undergone an unnecessary gastroduodenoscopy procedure. Clues that this dog had Addison's disease included the non-specific gastrointestinal signs, lack of a stress leukogram, and presence of non-regenerative anemia, hypocholesterolemia and hypoalbuminemia. It is important for clinicians to appreciate that dogs with Addison's disease can present with a wide variety of clinical signs. Affected dogs may have marked hypoalbuminemia and hypocholesteremia and present with clinical signs that are similar to other causes of protein-losing enteropathy in dogs such as inflammatory bowel disease, lymphangiectasia and lymphoma. Dogs diagnosed with atypical Addison's disease should be carefully monitored because they may have progression of their disease and develop electrolyte abnormalities. This usually happens within 12 months of the diagnosis of primary hypoadrenocorticism.

Key point

Not all dogs with primary canine Addison's disease have hyperkalemia and hyponatremia at the time of diagnosis. Careful monitoring is required to make sure that electrolyte abnormalities are detected and treated appropriately.

Please refer to the complete Important Safety Information located on page 1.

TABLE 1

Complete blood count results

Analyte	Value	Reference range	Units
Total protein	4.5	6.0-8.0	g/dl
Hematocrit	26.9	37-55	%
Hemoglobin	9.23	12-18	g/dl
Red blood cells	4.06	5.5-8.5	X 10^6 microL
MCV	66.2	60-75	fl
MCHC	34.3	32-36	g/dl
White blood cells	12.0	6-17	X 10^3/microL
Segmented neutrophils	9.6	3-12	X 10^3/microL
Lymphocytes	1.68	1-5	X 10^3/microL
Monocytes	0.48	0.15-1.35	X 10^3/microL
Eosinophils	0.24	0.1- 1.25	X 10^3/microL
Platelets	320	200-900	X 10^3/microL
Reticulocyte count	64.96		Cells/microL

TABLE 2

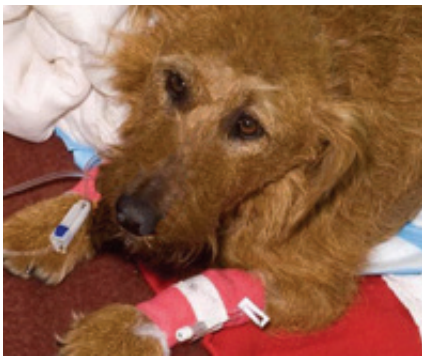
Selected values from chemistry panel

Analyte	Value	Reference range	Units
Phosphorus	4.9	2.2-7.9	mg/dl
BUN	21	7 - 32	mg/dl
Creatinine	0.8	0.5 – 1.5	mg/dl
Sodium	140	138 - 148	mmol/l
Potassium	4.3	3.5 – 5.0	mmol/l
Chloride	121	105 - 117	mmol/l
Calcium	9.4	9.7-12.3	mg/dl
Total protein	4.9	4.8-6.9	g/dl
Albumin	1.4	2.3-3.9	g/dl
Globulin	3.4	1.7-3.8	g/dl
Cholesterol	84	135-301	mg/dl
Glucose	71	67-132	mg/dl

Anisocytosis 1+, Poikilocytosis 1+ Polychromasia noted, reactive lymphocytes noted.

CASE IN BRIEF

Diagnosis and Treatment of Canine Addison's Disease



Signalment
18-month-old Female Spayed Irish Terrier

History
Owner reports a 2-day history of decreased activity, depression and anorexia. A similar episode two months previously resolved with supportive care. The dog has not received any medications and was last vaccinated six months ago.

Physical examination
The dog was laterally recumbent and lethargic. Mucous membranes were injected, hyperemic, and tacky. Capillary refill time was prolonged at three seconds. Body temperature was low at 95.1°F, the dog was bradycardic, with heart rate and pulse of 48 beats per minute. Respiratory rate was normal (16 breaths per minute). Body weight was 16 kg and body condition score was 5/9. Blood pressure was too low to measure.

Diagnostic plan
Blood was collected and an ACTH stimulation test performed. The bladder was too small to collect urine. Blood abnormalities (CBC, serum chemistry panel) included hemoconcentration, severe hyperkalemia (10.5 mmol/l) hyponatremia (128 mmol/l), and azotemia (BUN 201 mg/dl, creatinine 6.9 mg/dl) (see tables 3 and 4). An ECG showed atrial standstill. P waves were absent and the duration of the QRS complex and QT interval were prolonged (see figure 5).

Initial treatment plan
Initial treatment for the hypovolemic shock and hyperkalemia included IV catheter placement and fluid resuscitation with an IV saline bolus followed by a saline infusion (6 ml/kg/hour). Drugs administered included dextrose, insulin, calcium gluconate and bicarbonate to decrease the serum potassium concentration and protect the myocardium from the effects of hyperkalemia. The arrhythmia resolved and the heart rate normalized. Because of the clinical diagnosis of Addison's disease, the dog was also treated with IV dexamethasone (initial dose 0.2 mg/kg then 0.1 mg/kg in IV fluids), and one dose of Percorten-V (desoxycorticosterone pivalate injectable suspension) (2.2 mg/kg or 1 mg/lb IM).

Outcome
The ACTH stimulation test showed both a pre- and post-cortisol of < 1 µg/dl confirming the diagnosis of hypoadrenocorticism (Addison's disease). The dog responded well to treatment and was discharged on prednisone at a dose of 0.25 mg/kg PO q 24 hours with plans to taper the dose over the next few weeks to 0.1 mg/kg of prednisone or less. The dog was scheduled for a recheck visit in two weeks and follow up Percorten injection 25 days from presentation.

Veterinarian's comments
This case is a good example of the appropriate management of an acute presentation of Addison's disease. A delay in treatment would have resulted in death due to hyperkalemia. The severe bradycardia in the presence of hypovolemic shock suggested hyperkalemia even before laboratory results were available. In patients with severe hyperkalemia, strategies to rapidly decrease the potassium concentration (administration of dextrose, insulin and sodium bicarbonate) and to protect the myocardium (calcium gluconate) are needed. The history that included a previous less severe episode was typical for dogs with Addison's disease. Because Addison's disease was diagnosed on the history and the acute clinical presentation, Percorten-V (DOCP) was administered prior to receiving laboratory results. Other abnormalities that supported the diagnosis included azotemia and lack of a stress leukogram.

Key point

In a dog presenting with acute hypoadrenocorticism, immediate initiation of treatment, including Percorten-V administered IM at a starting dose of 2.2 mg/kg, prevented death from hyperkalemia.

Please refer to the complete Important Safety Information located on page 1.

TABLE 3

Complete blood count results

Analyte	Day 1	Reference range	Units
Total protein	6.6	6.0-8.0	g/dl
Hematocrit	62.8	37-55	%
Hemoglobin	21.4	12-18	g/dl
Red blood cells	9.06	5.5-8.5	x 10^6/µl
MCV	69	60-75	fl
MCHC	34	32-36	g/dl
White blood cells	9.7	6-17	x10^3/µl
Bands	0	0-0.3	x10^3/µl
Segmented neutrophils	6.82	3-12	x10^3/µl
Lymphocytes	1.61	1-5	x10^3/µl
Monocytes	0.19	0.15-1.35	x10^3/µl
Eosinophils	0.85	0.1-1.25	x10^3/µl
Nucleated red blood cells	0		/100wbc
Platelets	clumped		x10^3/µl
Reticulocyte count	ND	200-900	x10^3/µl
Morphology	Aniso 1+, Poik 1+		

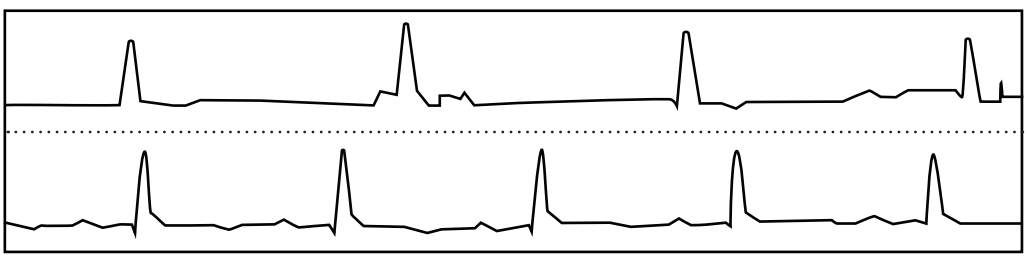
TABLE 4

Selected values from chemistry panel

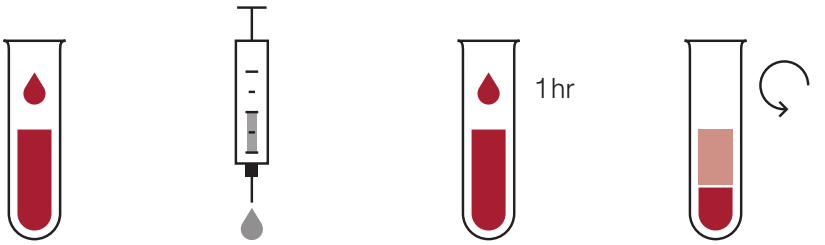
Analyte	Value		Reference range	Units
Phosphorus	23	↑	2.2-7.9	mg/dl
BUN	201	↑	7 - 32	mg/dl
Creatinine	6.9	↑	0.5 – 1.5	mg/dl
Sodium	128	↓	138 - 148	mmol/l
Potassium	10.5	↑	3.5 – 5.0	mmol/l
Chloride	95	↓	105 - 117	mmol/l

FIGURE 1

ECG tracing before and after treatment of hyperkalemia



Conducting the ACTH Stimulation Test



Step 1
Obtain baseline blood sample

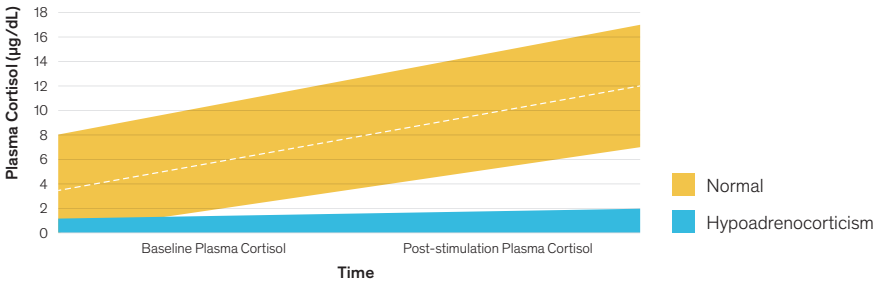
Step 2
Administer synthetic ACTH 5 µg/kg via IV or IM

Step 3
Take a post-stimulation blood sample 1 hour later

Step 4
Centrifuge both blood samples and submit serum to laboratory

Interpreting the results

A dog with Addison's Disease will show low baseline cortisol with little to no response to ACTH. A normal dog will have a normal response to ACTH.



Adapted from Feldman, E. 1989. "Adrenal Gland Disease." In S. J. Ettinger, Textbook of Veterinary Internal Medicine, 3rd Edition:1721-1770.

Percorten®-V
(desoxycorticosterone pivalate injectable suspension)

Please refer to the complete Important Safety Information located on page 1.

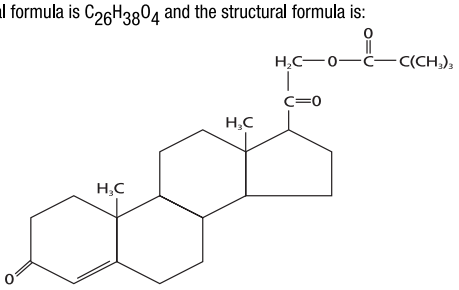
Elanco

Percorten™-V
(desoxycorticosterone pivalate injectable suspension)

PC3810H

CAUTION:
Federal (U.S.A.) law restricts this drug to use by or on the order of a licensed veterinarian.

DESCRIPTION:
The active ingredient in PERCORTEN-V is desoxycorticosterone pivalate (DOCP). It is a mineralocorticoid hormone and an analog of desoxycorticosterone. It is white, odorless, and stable in air. It is practically insoluble in water, sparingly soluble in acetone, slightly soluble in methanol, ether and vegetable oils. The molecular weight is 414.58. It is designated chemically as 21 (2,2-dimethyl-1-oxopropoxy)-pregn-4-ene-3,20-dione. The empirical formula is $C_{26}H_{38}O_4$ and the structural formula is:



PERCORTEN-V is a white aqueous suspension. Each ml contains 25mg desoxycorticosterone pivalate, 10.5mg methylcellulose, 3mg sodium carboxymethylcellulose, 1mg polysorbate 80 and 8mg sodium chloride with 0.002% thimerosal as preservative in water for injection.

CLINICAL PHARMACOLOGY:
Desoxycorticosterone pivalate (DOCP), like other adrenocorticoid hormones, is thought to act by controlling the rate of synthesis of proteins. It reacts with receptor proteins in the cytoplasm to form a steroid-receptor complex. This complex moves into the nucleus, where it binds to chromatin that results in genetic transcription of cellular DNA to messenger RNA. The steroid hormones appear to induce transcription and synthesis of specific proteins which produce the physiologic effects seen after administration.

DOCP is a long-acting ester of desoxycorticosterone acetate (DOCA) which is recognized as having the same qualitative effects as the natural mineralocorticoid hormone aldosterone.

The most important effect of DOCP is to increase the rate of renal tubular absorption of sodium. This effect is seen most intensely in the thick portion of the ascending limb of the loop of Henle. It also increases sodium absorption in the proximal convoluted tubule but this effect is less important in sodium retention. Chloride follows the sodium out of the renal tubule.

Another important effect of DOCP is enhanced renal excretion of potassium. This effect is driven by the resorption of sodium that pulls potassium from the extracellular fluid into the renal tubules, thus promoting potassium excretion.

DOCP also acts to increase extracellular fluid volume. The enhanced retention of sodium, chloride and bicarbonate, creates an osmotic gradient that promotes water absorption from the renal tubules. The extracellular fluid volume is supported. This expands the blood volume and improves the venous return to the heart and cardiac output. The expanded blood volume and increased cardiac output may result in elevated blood pressure. PERCORTEN-V prevents the life threatening hypotensive shock and pre-renal azotemia observed in animals suffering from hypoadrenocorticism.

The effects of PERCORTEN-V on electrolytes and extracellular fluid volume are dependent on a functioning kidney. Animals suffering from hypovolemia, pre-renal azotemia, and inadequate tissue perfusion must be rehydrated with intravenous fluid (saline) therapy, before starting PERCORTEN-V therapy. Primary renal disease should be ruled out before starting PERCORTEN-V therapy.

DOCP is an insoluble ester of desoxycorticosterone. The crystals are injected intramuscularly as a micro-crystalline depot where they slowly dissolve over time.

INDICATION:
For use as replacement therapy for the mineralocorticoid deficit in dogs with primary adrenocortical insufficiency.

WARNING:
Do not use this drug in pregnant dogs. Do not use in dogs suffering from congestive heart disease, severe renal disease or edema.

Keep this and all drugs out of the reach of children. In case of human consumption, contact a physician or Poison Control Center immediately.

PRECAUTIONS:
Some patients are more sensitive to the actions of PERCORTEN-V and may exhibit side effects in an exaggerated degree. Some patients may show signs of hypernatremia or hypokalemia. The dosage of PERCORTEN-V should be reduced in these patients. Concomitant use of PERCORTEN-V with potassium-sparing diuretics, such as spironolactone, may counter the effect of PERCORTEN-V because desoxycorticosterone pivalate and potassium-sparing diurectics exhibit opposing mechanisms of action.

Like other adrenocortical hormones, PERCORTEN-V may cause severe side effects if dosage is too high or prolonged. It may cause polyuria, polydipsia, increased blood volume, edema and cardiac enlargement. Excessive weight gain may indicate fluid retention secondary to sodium retention. PERCORTEN-V should be used with caution in patients with congestive heart disease, edema or renal disease.

ADVERSE REACTIONS (in controlled clinical field studies):
The following adverse reactions have been reported following the use of PERCORTEN-V: depression, polyuria, polydipsia, anorexia, skin and coat changes, diarrhea, vomiting, weakness, weight loss, incontinence, pain on injection and injection site abscess. Some of these effects may resolve with adjustments in dose or interval of PERCORTEN-V or concomitant glucocorticoid medication.

Post-Approval Experience, Rev. 2011:
The following adverse events are based on post-approval adverse drug experience reporting. Not all adverse events are reported to FDA-CVM. It is not always possible to reliably estimate the adverse event frequency or establish a causal relationship to product exposure using this data. The following adverse events are listed in decreasing order of reporting frequency in dogs: depression/lethargy, vomiting, anorexia, polydipsia, polyuria, diarrhea, facial/muzzle edema, weakness, urticaria and anaphylaxis. Anemia has been reported following DOCP administration. For a complete listing of adverse reactions for desoxycorticosterone pivalate injectable suspension reported to CVM see: http://www.fda.gov/AnimalVeterinary.

To report adverse effects, access medical information, or obtain additional product information call 1-888-545-5973. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or http://www.fda.gov/AnimalVeterinary/SafetyHealth.

EFFICACY:
PERCORTEN-V given intramuscularly at the appropriate dose and interval, is effective in replacing the mineralocorticoid deficit in dogs suffering from primary hypoadrenocorticism.

Results of two 75-day clinical studies in dogs with primary hypoadrenocorticism have demonstrated the clinical efficacy of PERCORTEN-V. Each dog received three doses of PERCORTEN-V (on days 0, 25 and 50).

The results are summarized below.

	Clinical Study Number 01	02
Number of Dogs	49	18
Average Diagnostic Values:		
Serum Sodium (mEq/L)	128.4	130.72
Serum Potassium (mEq/L)	7.28	7.47
Sodium/Potassium Ratio	18.09	17.86
ACTH Stimulation Test:		
Cortisol Resting (µg/dl)	0.28	0.68
Cortisol Post Stimulation (µg/dl)	0.27	1.34
Average PERCORTEN-V Dose (mg/lb):		
Day 0	0.97	0.99
Day 25	0.96	0.99
Day 50	0.94	0.97
Concomitant Glucocorticoid (Pred)	47%	39%

Sodium/Potassium Ratios		
Day 0	25.18	26.42
Day 14	36.36	–
Day 25	29.64	–
Day 39	34.94	–
Day 50	30.33	–
Day 64	35.30	–
Day 75	30.32	30.59
% Efficacy Therapy	96%	100%

Case Management:[1,2]
An accurate diagnosis of primary canine adrenocortical insufficiency is of paramount importance for treatment success and should be established before initiation of PERCORTEN-V therapy. While hyponatremia and hyperkalemia are highly suggestive of adrenocortical insufficiency, they are not pathognomonic. A definitive diagnosis can only be made with an ACTH stimulation test. At diagnosis, classic cases of canine adrenocortical insufficiency may include clinical signs. Those signs are anorexia, lethargy, depression, weakness, vomiting and/or regurgitation, weight loss, diarrhea and collapse, serum sodium values less than 135 mEq/L, serum potassium greater than 6 mEq/L, sodium/potassium ratios below 25:1, plasma or serum cortisol concentration less than 4 µg/dl pre-and-post ACTH administration. Once the diagnosis is made, immediate therapy must be given to normalize electrolyte imbalance, correct hypovolemic shock and re-establish normal homeostasis. Such therapy should include large volumes of intravenous physiologic saline, glucocorticoids (i.e., prednisolone, dexamethasone) at shock doses and PERCORTEN-V. Anemia (normocytic, normochromic) may be present at diagnosis, but not identified due to hemoconcentration. Rapid rehydration may reduce the circulating red blood cell count to life-threatening levels in animals with preexisting anemia. Once the acute crisis has passed, renal and cardiovascular function should return to normal. Patient monitoring and dose adjustments of PERCORTEN-V and glucocorticoids should be instituted at this time (see Dosage).

SAFETY:[3]
In a laboratory study the safety of PERCORTEN-V was established in five month old Beagle dogs. PERCORTEN-V was administered IM to 24 Beagles at 0, 2.2, 6.6 or 11 mg/kg of body weight daily over a consecutive 3-day period every 28 days (equivalent to a cumulative monthly dosage of 0, 6.6, 19.8 or 33 mg/kg) for 6 months. This resulted in no mortality or any significant effects on body weight, food consumption, and ophthalmic observations at any dose level. However, polyuria and polydipsia were noted and creatinine concentration decreased (14-89 mg/dl) in the 1X, 3X and 5X groups. Histopathological changes were only observed in the kidneys when PERCORTEN-V was administered at ≥ 6.6 mg/kg. The primary renal lesion consisted of glomerulonephropathy seen in all males at ≥ 6.6 mg/kg, in one female at 6.6 mg/kg, and in all females at 11 mg/kg. Other possible treatment related lesions in the kidney, observed sporadically in the 6.6 and 11.0 mg/kg groups, were tubular hyperplasia, inflammation and tubular dilatation. Glomerulonephropathy may possibly be attributed to the pharmacological effects of the drug although there were no clinical measurements assessed in this study. In conclusion, PERCORTEN-V was well tolerated, when administered at 2.2 mg/kg on three consecutive days in every 28-day period for six months.

DOSAGE:[1,2]
In treating canine hypoadrenocorticism, PERCORTEN-V replaces the mineralocorticoid hormones only. Glucocorticoid replacement must be supplied by small daily doses of glucocorticoid hormones (e.g., prednisone or prednisolone) (0.2 – 0.4 mg/kg/day).

Dosage requirements are variable and must be individualized on the basis of the response of the patient to therapy. Begin treatment with PERCORTEN-V at a dose of 1.0 mg per pound of body weight every 25 days. In some patients the dose may be reduced. Serum sodium and potassium levels should be monitored to assure the animal is properly compensated. Most patients are well controlled with a dose range of 0.75 to 1.0 mg per pound of body weight, given every 21 to 30 days.

The well-controlled patient will have normal electrolytes at 14 days after administration or may exhibit slight hyponatremia and hyperkalemia. This needs no additional therapy as long as the patient is active and eating normally. Watch closely for depression, lethargy, vomiting or diarrhea which indicate a probable glucocorticoid deficiency.

At the end of the 25-day dosing interval, the patient should be clinically normal and have normal serum electrolytes. Alternatively, they may have slight hyponatremia and slight hyperkalemia. This constellation of signs indicate that the dosage and dosage interval should not be altered.

If the dog is not clinically normal or serum electrolytes are abnormal, then the dosage interval should be decreased 2-3 days.

Occasionally, dogs on PERCORTEN-V therapy may develop polyuria and polydipsia (PU/PD). This usually indicates excess glucocorticoid, but may also indicate a PERCORTEN-V excess. It is prudent to begin by decreasing the glucocorticoid dose first. If the PU/PD persists, then decrease the dose of PERCORTEN-V without changing the interval between doses.

Please note: Failure to administer glucocorticoids is the most common reason for treatment failure. Signs of glucocorticoid deficiency include depression, lethargy, vomiting and diarrhea. Such signs should be treated with high doses of injectable glucocorticoids (prednisolone or dexamethasone), followed by continued oral therapy 0.2 – 0.4 mg/kg/day. Oral supplementation with salt (NaCl) is not necessary with animals receiving PERCORTEN-V.

Guide to Maintenance Therapy
Starting Dose:
DOCP 1 mg/lb every 25 days
Prednisone 0.2 - 0.4 mg/kg/day

Guides for Adjustment:
Clinical Problem/Solution
Polyuria/Polydipsia
→ decrease prednisone dose first,
→ then decrease DOCP dose,
→ do not change DOCP interval

Depression, lethargy, vomiting or diarrhea
→ increase prednisone dose

Hyperkalemia, Hyponatremia
→ decrease DOCP interval 2-3 days

ADMINISTRATION:
Before injection, shake the vial thoroughly to mix the microcrystals with the suspension vehicle. PERCORTEN-V suspension is to be injected intramuscularly. Care should be used to prevent inadvertent intravenous injection, which may cause acute collapse and shock. Such animals should receive immediate therapy for shock with intravenous fluids and glucocorticoids.

Once vial is broached, product should be used within 4 months.

HOW SUPPLIED:
Multiple-Dose Vials, 4 ml, each ml containing 25 mg desoxycorticosterone pivalate (DOCP), 10.5 mg methylcellulose, 3 mg sodium carboxymethylcellulose, 1 mg polysorbate 80, and 8 mg sodium chloride with 0.002% thimerosal added as preservative in water for injection. Packed one vial per carton.

STORAGE:
Store at controlled room temperature 25ºC with excursions between 15-30ºC (59-86ºF) permitted. Protect from light. Protect from freezing.

References:

1. Canine and Feline Endocrinology and Reproduction. Second Edition (1996), E. C. Feldman and R. W. Nelson, W. B. Saunders Co., New York and Third Edition (2004) Saunders/Elsevier, USA.
2. Textbook of Veterinary Internal Medicine. Fourth Edition, S. J. Ettinger and E. C. Feldman editors, W. B. Saunders Co., New York, 1995.
3. Toxicity of desoxycorticosterone pivalate given at high doses to clinically normal Beagles for six months, E. Chow, W. R. Campbell, J. C. Turnier, R.C. Lynn and K. L. Pavkov, Am. J. Vet. Res. 54(11):1954-1961, 1993.

Manufactured for: Elanco US Inc.
Greenfield, IN 46140, USA

NADA # 141-029, Approved by FDA.

PC3810H